Clinical Investigation Plan

CP352

An exploratory investigation of the effects of single use vs. reuse catheters in intermittent catheterization

June 2022 – March 2023

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CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	Initial document based on template 9.0
2.0	[redacted]	Section 17.2 Compensation for participating in the clinical investigation: Has been updated due to review from VMK
3.0	[redacted]	Front page: Timelines has been updated Synopsis of the clinical investigation: Expected duration of the clinical investigation: Timelines has been updated Section 5.8 Total expected duration of the clinical investigation: Timelines has been updated

SYNOPSIS OF THE CLINICAL INVESTIGATION

Title: An exploratory investigation of the effects of single use vs. reuse catheters in intermittent catheterization

The overall aim of the investigation is to investigate the effect of repeated reuse of intermittent urinary catheters and to observe the impact of switch from single use to multiple reuse catheters.

Throughout the investigation, the impact of switch from single use to multiple reuse catheters will be observed and compared with respect to health-related quality of life (HR-QoL), satisfaction, perception, and preference in female and male catheter-users, who use clean intermittent catheterization (CIC) for bladder management.

Furthermore, the investigation intends to identify microbial contamination of reused catheters and compare proportions to a control single use catheter.

Test products

The CP352 investigational device is the CE-marked CLINY reuse catheter (CLINY Self-Catheterization Set) which is a reusable catheter made of 100% silicone rubber to be reused for a maximum of 28 days before disposal.

Intended use and purpose

The device is to be inserted temporally into the patient´s urethra and bladder for urination (see instruction for use in Appendix A). For this investigation the device is to be inserted temporally into the participating subjects' urethra for drainage of the urine bladder.

Objectives

The objective is to compare health-related quality of life (HR-QoL) when using single use catheters with reuse catheters.

The **primary objective** is to investigate whether the reuse catheter CLINY can impact health-related quality of life in CIC users when compared to single use.

The **secondary objectives** are to evaluate whether the reuse catheter CLINY can impact satisfaction, perception, preference, and microbial contamination when compared to single use.

Design of the investigation

The investigation is designed as an open-labelled, single-arm investigation including subjects currently using single use catheters.

The cohort will in total consist of 40 CIC users, who must test reusable catheters. Each subject will participate for approximately 4 weeks, including up to 3 site visits and 3 phone visits, overseen by the investigator, or delegate, within the 4-weeks home test period.

Expected duration of the clinical investigation

The investigation will be conducted from June 2022 through March 2023.
Each subject will undergo screening and baseline visits, which can be performed the same day, followed by a 4-week (28-days test period). When the 28-days test period is completed, a termination visit will be performed.

Primary, secondary, and exploratory endpoints

Primary endpoint:

- Health-related quality of life (HR-QoL) measured by the intermittent self-catheterization questionnaire, (ISC-Q) index score

Secondary endpoints:

- Adverse events

Exploratory endpoints:

- Intermittent Catheterization Satisfaction (InCaSa) questionnaire score
- Perception questions (evaluated on a 6-point scale)
- Total catheter-associated bacterial count (CFU/mL)
- Number of bacterial-positive catheter samples

Population and subjects

The clinical investigation will be conducted in a total of 40 subjects male and female CIC users recruited at multiple clinical investigational sites in Denmark. To be included in the investigation, the subjects must comply with the selected criteria described below.

Inclusion and exclusion criteria:

Inclusion criteria	Exclusion criteria
1. ≥18 years of age and has full legal capacity	1. Participation in any other clinical intervention study during this investigation
2. Signed informed consent form	2. Previous participation in this investigation
3. Use clean intermittent catheterization to the greatest extent possible (at least three times daily) for at least the last 1 month prior to inclusion	3. Any known allergies towards ingredients in the investigational device
4. Ability (assessed by the investigator) and willingness to participate in a 4-week study period with at least three catheterizations a day using the investigational test product	4. Symptoms of UTI at time of inclusion, as judged by the investigator
5. Self-catheterize using a single use hydrophilic coated catheter for at least 1 month prior to inclusion	5. Antibiotic treatment within 2 weeks prior to the Baseline visit (V1)
	6. Pregnancy
	7. Breastfeeding

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 18.2
AE	Adverse Event	See section 18.1
SADE	Serious Adverse Device Effect	See section 18.4.1
USADE	Unanticipated Serious Adverse Device Effect	See section 18.4.2
CIC	Clean Intermittent Catheterization	
CIP	Clinical Investigation Plan	
CISC	Clean Intermittent self-Catheterization	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection, see section 7.3 and section 11 Data Management
CM	Clinical Manager	
DD	Device deficiency	
EC	Ethics Committee	
IFU	Instruction for Use	
ITT	Intention to Treat	
MDR	Medical Device Regulations	
PI	Principal Investigator	Qualified person responsible for conducting the clinical investigation at an investigation site. If the clinical investigation is conducted by a team of individuals at an investigation site, the PI is the responsible leader of the team. Whether this is the responsibility of an individual or an institution can depend on national regulations.

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1. List of personnel involved in the Investigation

1.1. Sponsor representatives

COORDINATING CLINICAL MANAGER	DIRECTOR OF CLINICAL OPERATIONS
[redacted]	
PROJECT MANAGER	DATA MANAGEMENT SPECIALIST
[redacted]	
DIRECTOR OF CLINICAL STRATEGIES	PRINCIPAL BIOSTATISTICIAN, CLINICAL STRATEGIES
[redacted]	
CHIEF PRINCIPAL SCIENTIST PRE-CLINICAL	MEDICAL WRITER
[redacted]	

In case of emergency, please contact Clinical Manager, [redacted] from the sponsor representatives list above

1.1.1. Investigators

Site 1 – DK001 Coordinating Principal Investigator	Site 2 – DK002 Principal Investigator	Site 3 – DK003 Principal Investigator
[redacted]		

2. Rational/justification for conducting the clinical investigation

In patients with neurogenic or non-neurogenic bladder dysfunction, intermittent catheterization (IC) is a well-accepted tool for bladder management,[1-3] ensuring patient independence and improved quality of life. [4-6]

To minimize the risk of urinary tract infections (UTIs), the use of sterile, single use catheters has for many years been the recommended standard of care.[7,8] However, based on cost and an environmental agenda, a push for reuse catheters has emerged.[9,10] International associations do not currently endorse catheter reuse due to the lack of standardized cleaning and reuse recommendations and a concern of decreased compliance, unsafe practice and increased risk of UTIs.[11] There is at present a lack of solid evidence with respect to risk of UTIs associated with single use vs. reuse, though one recent metanalysis including > 900 users found single use catheters to be the only catheter associated with reduced UTI rate.[12]

Deciphering the influence of catheter per se is complicated by the highly complex and multifactorial causalities associated with UTIs in IC users,[13] however, a recent study demonstrated significant bacterial contamination on reuse catheters.[14] Also, there was an end-study preference towards single use and increased health-related (HR) QoL, when changed from reuse to single use catheter.[14] These results align well with user concerns, namely, the risk of UTIs and the burden of repeated daily cleaning procedures.[15]

In alignment with these concerns, the aim of the present investigation is to investigate potential user challenges and level of catheter contamination, associated with introducing re-use catheters in a patient population accustomed to single use catheters. Thus, addressing the influence of catheter choice on HR-QoL and treatment satisfaction, the primary aim of this investigation is to analyse single use vs. re-use, using validated IC-specific questionnaires. To better evaluate the risk of potential catheter contamination at time of catheter reuse, the secondary aim is to analyse bacterial colonization after catheter cleaning and storage, just prior to catheterization.

The overall aim of the investigation is to investigate the effect of repeated reuse of intermittent urinary catheters and to observe the impact of switch from single use to multiple reuse catheters.

3. Objectives and hypotheses of the clinical investigation

3.1. Objectives

The **primary objective** is to investigate whether the reuse catheter CLINY can impact health-related quality of life in CIC users when compared to single use.

The **secondary objectives** are to evaluate whether the reuse catheter, CLINY can impact satisfaction, perception, preference, and microbial contamination when compared to single use.

3.2. Hypotheses

No formal success criteria are applied in this investigation. The investigation will provide valuable insight into performance and evaluation of effects, impact, and comparison of a switch from single use catheters to reusable catheters.

4. Investigational device

The investigational device is the CE-marked reusable Self-Catheterization Set, named CLINY. The Set is a Self-Catheterization Set produced by the Japanese company Create Medic co., LTD.

4.1. Description of the investigational device

The CLINY Self-Catheterization Set consists of four non-sterile parts:

- A foldable catheter case of polypropylene, silicone rubber (can be folded into a small size)
- A cap of polypropylene, silicone rubber
- A catheter of silicone rubber
- An outer case to carrying with the catheter case

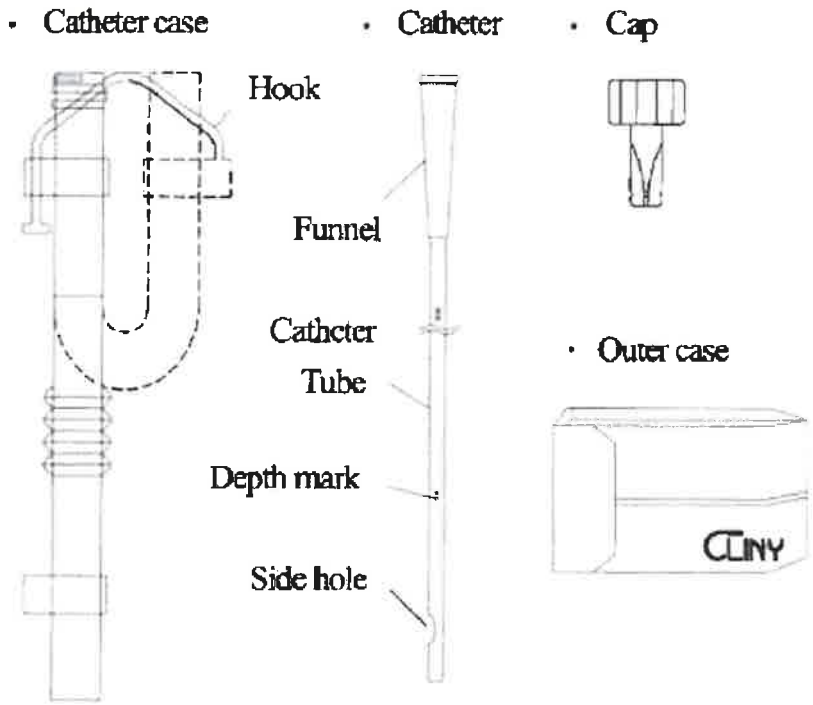

Figure 1: CLINY Self-Catheterization Set

The following catheter sizes for female and male will be available in the investigation. See Table 1.

Table 1: Investigational devices available in the investigation

	Size	Length	Content
Female	12 FR	165 mm	CLINY Self-Catheterization Set
Male	12 FR	395 mm	CLINY Self-Catheterization Set
Male	14 FR	395 mm	CLINY Self-Catheterization Set

4.2. Manufacturing

Responsible for manufacturing the investigational device:

CREATE MEDIC CO., LTD.
Head Office
5-25 Chigasakiminami 2-Chome, Tsuzuki-ku,
Yokohama Kanagawa,
224-0037, Japan.

4.3. Identification and traceability of the device

The investigational device is the CE marked physical test product identified as CLINY Self-Catheterization Set. The investigational product will be used according to the intended use and will be stored safe and controlled at site. The Investigator Site File includes an accountability log for the control of the investigational device.

All the investigational devices are labelled as per regulations and include "Exclusively for clinical investigational use" (Udelukkende til klinisk afprøvning). The devices are also identified with an investigation number, product name/code, and item/Lot number and accounted through a master sponsor accountability log.

Upon EC approval, the investigational devices will be shipped to the Principal Investigator or delegate(s). Additionally, all investigational devices will be accounted for and documented on a site accountability log. All used and unused devices will be returned to Coloplast.

4.4. Intended use of the device in the clinical investigation

The investigational test product is a Self-Catheterization Set for re-use in 28 days and is only to be used for drainage of the bladder through the urethra. The product is a MDR class 1 device.

4.5. Intended population for the device

The intended population for this investigational device is males and females who are depending on clean intermittent catheterization for bladder management.

4.6. Handling of the investigational device

Handling of the CLINY Self-Catheterization Set with reusable catheter is described in detail in the instruction for use (IFU), which is included in all boxes with the investigational device.
See the IFU in Appendix A.

The Principal Investigator and delegate(s) will receive training by the sponsor in handling and correct use of the investigational device. The PI or delegate will train the subject in the correct use of the investigational device according to the IFU.

4.7. Total number of devices intended for the clinical investigation

Each subject will be supplied with one CLINY Self-Catheterization Set, and cleansing products as described below:

1 CLINY Self-Catheterization Set:

- 1 catheter case with a cap
- 1 outer case
- 1 bottle of Milton cleansing solution
- Optilube, sterile lubricating gel

In case of a damaged or missed CLINY catheter, the subject will be distributed a new CLINY Self-Catheterization Set from site. Sponsor must be reported if a replacement of a new CLINY Self-Catheterization Set is needed, and the replacement must be reported in the eCRF. The replaced CLINY as well as the new CLINY must be collected by the site and sent for laboratory assessments by the end of use.

To ensure that the site has enough supplies, more products than needed will be provided by sponsor to the site. All products will be accounted for both prior and after use.

5. Design of the clinical investigation

5.1. General

The investigation is designed as an open-labelled, single-arm investigation, in which the reuse CLINY catheter will be compared to single use catheters at baseline.

The study design includes an initial evaluation of a cohort of catheter users who currently practice hydrophilic single use clean intermittent catheterization. The cohort will be followed for 4 weeks (28 days) when switching to multiple reuse catheters.

The test period of 4 weeks will consist of up to 3 site visits and 3 phone visits within a 4-week test period. Subjects using single use catheters for bladder management will use one distributed CLINY Self-Catheterization Set during the test-period. The expected duration of the total test-period is 28 days.

In total, 40 subjects will be included in the investigation. Each subject will undergo a Screening Visit (V0), a Baseline Visit (V1), 3 phone calls (V2, V3 and V4) and a Termination Visit (V5) carried out by the Principal Investigator (PI), or delegate. Visit 0 and 1 can be performed on the same day.

At a scheduled Screening Visit (V0), the subject will be verbally informed about the investigation, where the PI or delegate will give information about the investigation, the content and what it involves when participating in the investigation and the eligibility criteria. This information can be performed as a phone call if needed and the subject will be distributed a Subject Information Form/Informed Consent Form/ (SIF/ICF) by mail.

At the scheduled Baseline Visit (V1), the subject receives additional information if needed and the in- and exclusion criteria will be reviewed. See section 6.2 for recruitment and enrolment.

The Screening Visit (V0) and Baseline Visit (V1) can be performed the same day.
If the subject wishes to reconsider his/her participation at V0 after another oral review of the content of the investigation, the subject has the rights to wait minimum 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation a V1 will be scheduled unless performed the same day as the Screening Visit (V0).

The subject is included in the investigation upon signed informed consent at the Baseline visit (V1).
The Baseline Visit (V1) can be conducted at the latest, 3 days after V0.

At V1, all baseline information will be collected by the PI or delegate (see flow chart, Table 5).

The subject will complete questionnaires on a paper form and the investigator or delegate will report the assessments in an electronic data base, electronic Case Report Form (eCRF).

The subject will be instructed in use of the investigational test product, CLINY Self-Catheterization Set, according to the IFU (Appendix A).

A phone call (V2) will be conducted 7 days (+/- 1 day) after V1, a phone call (V3) will be conducted 14 days (+/-1 day) after V1, and a phone call (V4) will be conducted 21 days (+/-1 day) after V1.
At the time of the phone calls the subject will be reminded of the instructions for using the investigational device, CLINY Self-Catheterization Set, review of AE´s, review concomitant medication, evaluate use of single use catheters (protocol deviations), average number of daily catheterizations with CLINY and results of a same day urine dipstick will be assessed as well. The investigator or delegate will report the assessments in the eCRF.

The Termination Visit (V5) will be conducted 28 days (+3 days) after V1 unless a situation occurs where a subject terminates earlier than expected. If this is the case the subject will as the last visit have the termination visit performed (V5) including all assessments in Visit 5.

The subject will bring the used CLINY Self-Catheterization Set at the Termination Visit, and the PI or delegate will collect the used CLINY Self-Catheterization Set for laboratory analysis. The subject will complete Termination Visit (V5) questionnaires in a paper form and the investigator or delegate will report the assessments in the eCRF.

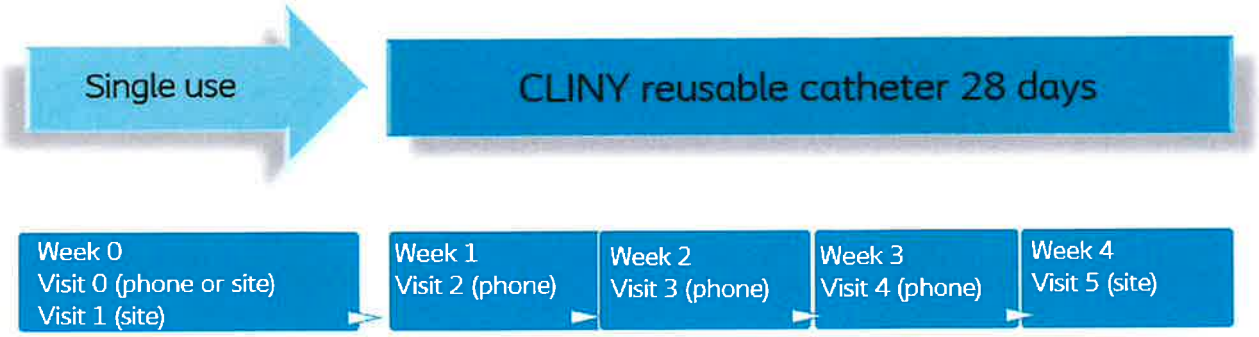

Figure 2: Design of the Clinical Investigation

5.2. Primary endpoint

Primary endpoint:

- Health-related quality of life (HR-QoL) measured by intermittent self-catheterization questionnaire, (ISC-Q) index score at Baseline Visit (V1) and at the termination Visit (V5)

5.3. Secondary and exploratory endpoints

Secondary endpoints:

- Adverse events

Exploratory endpoints:

- Satisfaction of intermittent catheterization measured by the InCaSa questionnaire score
- Perception questions (evaluated on a 6-point scale)
- Total catheter-associated bacterial count (CFU/mL)
- Number of bacterial-positive catheter samples

See Appendix H for endpoints and assessments.

5.4. Rationale for selection and measurement of endpoints

The primary as well as part of the exploratory endpoints and assessments are subjective and have been selected as they are considered essential parameters to evaluate the effects of repeated reuse of catheters and for the observation on the impact of a switch from single use to reusable catheters.

To evaluate the primary endpoint HR-QoL, the ISC-Q questionnaire will be applied. The ISC-Q [16] is a newly developed and validated patient reported outcome questionnaire that evaluates aspects of quality of life specific to the needs of patients with neurogenic bladder disorders who perform CIC. The questionnaire consists of 24 items categorized in 4 domains, including ease of use, convenience, discreetness, and psychosocial well-being. Each item is rated on a 5-point Likert scale.

The secondary as well as part of the exploratory endpoints are objective and are essential to investigate the effects of repeated reuse of catheters and for the observation on the impact of a switch from single use to reusable catheters as well as to ensure safety.

To evaluate the exploratory endpoint, satisfaction of intermittent catheterization, the InCaSa Questionnaire will be applied (InCaSa-Intermittent Catheterization Satisfaction Questionnaire) [17].

5.5. Demography and potential compromising factors

The following baseline data will be collected and reported at the Baseline Visit (V1) by the investigator or delegate:

- Date of informed consent
- Date of visit
- Age
- Height (in cm)
- Weight (in kg)
- Gender (Male/Female)
- Concomitant medication
- Reason for using intermittent catheterization
    - Spina cord injury
    - Multiple sclerosis
    - Spina Bifida
    - Benign Prostatic Hyperplasia
    - Others (text)

- When did you start using a catheter? (months/years)
- Current single use catheter (at time of enrolment)
    - Brand
    - Product name
    - Item number

- Single use catheter size at time of enrolment
- Average number of catheters used per day during the last 1 month
- Time spent on each catheterization from preparation to storage/disposal (in minutes)
- Handedness
- Urethral sensation
- Hand dexterity

5.6. Equipment/methods and timing for assessing the variables

The primary endpoint is evaluation of HR-QoL assessed at Baseline Visit (V1) based on use of the single use intermittent catheterization and assessed after 28 days at Termination Visit (V5) based on use of the reuse catheter. HR-QoL will be measured by the ISC-Q index score.
The secondary endpoint will be an evaluation of adverse events from time of signed informed consent and throughout the test period.

The exploratory endpoints will be collected with satisfaction questionnaire score and perception questions at visit 1 and visit 5.

Evaluation of intermittent catheterization satisfaction assessed at Baseline Visit (V1) and after 28-days of using the re-use catheter CLINY, at the Termination Visit (V5). For this assessment the InCaSA – Intermittent Catherization Satisfaction Questionnaire will be used.

Evaluation of intermittent catheterization related to perception will be assessed at Baseline Visit (V1) and after 28-days of using the reuse catheter CLINY, at the Termination Visit (V5). For this assessment, perception questions on a 6-point scale will be used for measuring of this endpoint.

Evaluation of total catheter-associated bacterial count and number of bacterial-positive catheter samples:

In a laboratory at Coloplast the total catheter-associated bacteria count (CFU/mL) will be assessed for all CLINY catheters collected at Termination Visit (V5). The number of bacterial-positive catheter samples will also be assessed, where positive is defined as presence of any detectable concentration. The data will be compared to a baseline evaluation of the CLINY catheter-associated bacterial count and number of bacterial-positive catheter

samples. In total 6 single use hydrophilic coated catheters taken directly from packages will be assessed, thus no bacteria are expected on the samples.

See Flowchart table 5 for further information regarding timing of endpoint data capture.

5.7. Blinding

(Not applicable)

5.8. Total expected duration of the clinical investigation

The dates below are approximate, and no subjects will be enrolled before all required approvals have been obtained. If changes are required, EC will be notified.

- First subject enrolled (06/2022)
- Last subject enrolled (02/2023)
- Last subject completed (03/2023)
- Final report (04/2023)

6. Clinical Investigation population

The clinical investigation will be conducted in 40 subjects enrolled in multiple clinical investigation sites. The enrolment is competitive.

To allow for statistically significant data, a minimum of 20 eligible completed subjects in multiple clinical investigation sites will be adequate for obtaining indications on the effects of repeated reuse of catheters, hence the aim for this investigation is 20-40 completers.

Considering a drop-out rate of 50 %, the total number of subjects to be enrolled must be 40.

Recruitment and discontinuation will be followed very closely, and all replacements evaluated on an ongoing basis depending on both number of discontinued subjects and the time the subjects participated in the investigation. As a minimum sponsor will make a status on the recruitment strategy every month or at least when half of the subjects have been recruited.

The aim is to keep the LPO date. If concerns of high dropout rate recruitment/retention arise and status will be discussed by sponsor.

6.1. Eligibility criteria

To be included in the investigation, the subjects must comply with the selection criteria described below

6.1.1. Inclusion criteria

Table 2: Inclusion criteria

Inclusion criteria	Justification
1. ≥ 18 years of age and has full legal capacity	To meet Helsinki declaration
2. Signed informed consent form	To meet Helsinki declaration
3. Use clean intermittent catheterization to the greatest extent possible (at least three times daily) for at least the last 1 month prior to inclusion	To ensure subjects are familiar with CIC use
4. Self-catheterize using a single use hydrophilic coated catheter for at least 1 month prior to inclusion	To ensure subjects are familiar with CIC use
5. Ability (assessed by the investigator) and willingness to participate in a 4-week study period with at least three catheterizations a day using the investigational test product	To ensure sufficient data for successful completion of the investigation

6.1.2. Exclusion criteria

Table 3: Exclusion criteria

Exclusion criteria	Justification
1. Participation in any other clinical intervention study during this investigation	To eliminate unintentional effects from other devices/medicines on the investigation's data
2. Previous participation in this investigation	To ensure data are not recorded twice
3. Symptoms of UTI at time of inclusion, as judged by the investigator	To ensure safety and integrity of results
4. Any known allergies towards ingredients in the investigational device	To ensure safety and integrity of results
5. Antibiotic treatment within 2 weeks prior to the Baseline Visit (V1)	To ensure integrity of results
6. Pregnancy	Even though the ingredients and recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown
7. Breastfeeding	Even though the ingredients and recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown

6.1.3. Pregnancy and breastfeeding

All female subjects with childbearing potential (they have at least one period during the last 12 months), must at V1 confirm that they are not pregnant or breastfeeding. A urine pregnancy test will be performed with a dipstick at site for confirmation. They will also be informed that no pregnancy is allowed during the investigation.

If the subject becomes pregnant during the investigation, it is important, that the subject informs the investigator or delegate immediately.

6.2. Recruitment and enrolment

Recruitment of potential subjects will begin once approval have been obtained from the Ethics Committee (EC). It is estimated that the recruitment process will be completed within 6 months.

Table 4: Overview of the recruitment process

Recruitment method	Outpatient clinic/hospital	Advertising	Coloplast Database
Potential subjects	Recruitment will go through the outpatient clinic at the hospital site. Potential subjects are identified by the following searching criteria: • ≥ 18 years of age • Use clean intermittent catheterization to greatest extent possible (at least three times daily) for at least the last 1 month prior to inclusion • Self-catheterize using a single use hydrophilic coated catheter for at least 1 month prior to inclusion • Ability and willingness to participate in a 4-week study period	Recruitment will go through an advertisement in relevant magazines. In the advertisement the following searching criteria are stated: • ≥ 18 years of age • Use clean intermittent catheterization to greatest extent possible (at least three times daily) for at least the last 1 month prior to inclusion • Self-catheterize using a single use hydrophilic coated catheter for at least 1 month prior to inclusion • Ability and willingness to participate in a 4-week study period In the advertisement potential subjects are asked to contact the coordinating PI for further information.	Recruitment will go through Coloplast Database and assessing potential subjects are identified by the following searching criteria: • ≥ 18 years of age • Use intermittent self-catheterization.
First contact	The potential subjects will be contacted by mail, phone call or contacted during a planned visit in the outpatient clinic at the hospital. If a subject is eligible and interested in participating in the investigation upon a short introduction, then written information about the investigation (Subject Information Form /Informed Consent Form) will be distributed to the subject. The Principal Investigator or delegate will invite the subject to a Screening Visit (V0).	The potential subjects will mail or call the Coordinating Principal Investigator. If a subject is eligible and interested in participating in the investigation upon a short introduction, then written information about the investigation (Subject Information Form /Informed Consent Form) will be sent to the subject and the subject will be re-directed to a recruiting site near the subjects' home for a potential Screening Visit (V0).	Potential subjects from the database will be contacted by phone or mail by the Principal Investigator or delegate. If subjects are eligible and interested in participating upon a short introduction, then written information about the investigation (Subject Information Form /Informed Consent Form) will be sent to the subject before a potential Screening Visit (V0).

Recruitment method	Outpatient clinic/hospital	Advertising	Coloplast Database
Screening Visit (V0)	At the scheduled Screening Visit (V0) the Principal Investigator or delegate will introduce the investigation and review the inclusion and exclusion criteria. If the subject wishes to reconsider his/her participation at V0, the subject has the rights to wait minimum 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation a Baseline Visit (V1) will be scheduled unless performed the same day as the Screening Visit. The Screening Visit can be formed at the site or as a phone call. If the subject does not meet the inclusion criteria or meet the exclusion criteria, this will be registered at the Subject Pre-Screening Log.	At the scheduled Screening Visit (V0) the Principal Investigator or delegate will introduce the investigation and review the inclusion and exclusion criteria. If the subject wishes to reconsider his/her participation at V0, the subject has the rights to wait minimum 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation a Baseline Visit (V1) will be scheduled unless performed the same day as the Screening Visit. The Screening Visit can be formed at the site or as a phone call. If the subject does not meet the inclusion criteria or meet the exclusion criteria, this will be registered at the Subject Pre-Screening Log.	At the scheduled Screening Visit (V0) the Principal Investigator or delegate will introduce the investigation and review the inclusion and exclusion criteria. If the subject wishes to reconsider his/her participation at V0, the subject has the rights to wait minimum 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation a Baseline Visit (V1) will be scheduled unless performed the same day as the Screening Visit. The Screening Visit can be formed at the site or as a phone call. If the subject does not meet the inclusion criteria or meet the exclusion criteria, this will be registered at the Subject Pre-Screening Log.
Baseline Visit (V1)	If the subject decides to participate and it is certain that it is understood what the investigation entails, the subject will be asked to sign the SIF/ICF. When the SIF/ICF is signed the subject is considered included in the investigation.	If the subject decides to participate and it is certain that it is understood what the investigation entails, the subject will be asked to sign the SIF/ICF. When the SIF/ICF is signed the subject is considered included in the investigation.	If the subject decides to participate and it is certain that it is understood what the investigation entails, the subject will be asked to sign the SIF/ICF. When the SIF/ICF is signed the subject is considered included in the investigation.

6.3. Subject withdrawal criteria

The subject is allowed to withdraw from the investigation at any time for whatever reason without any consequences for their future treatment outside the clinical investigation. The Investigator may withdraw a subject from the investigation at any time if they judge it to be the subject's interest.

The investigator must withdraw a subject from the investigation due to:

- Major noncompliance with the CIP impacting the scientific integrity of the investigation
- If subject's safety and wellbeing is compromised by further participation
- Subjects lost to follow-up. At least three documented attempts will be made to verify subjects lost to follow-up

All replacements can be made by sponsors decision and site must contact the Clinical Manager for replacement of a subject.

A subject who is withdrawn from the investigation, for any reason, will be encouraged to contact the investigator if problems arise that the subject believes are related to the clinical investigation. Subjects who have not experienced any adverse events will not be followed up.
For subjects who experience adverse events, se Section 18.1.

If a subject shows symptom(s) of UTI, as judged by the investigator, after the subject has been included in the investigation, the subject must be examined and treated according to sites standard of care or advised by investigator or GP. If antibiotic treatment is needed the subject must be withdrawn from the investigation and Termination Visit (V5) performed as soon as possible.

The subject must be advised to stop using the reusable catheter (CLINY Self-Catheterization Set) PRIOR to start of the antibiotic treatment. The subject must also be advised to save the CLINY catheter in the CLINY Self-Catheterization set and bring it to site for the Termination Visit.

The subject can return for a new scheduled visit V1 in cases where an UTI is detected after inclusion but prior to start of the test period with CLINY Self-Catheterization Set. The subject must be terminated as a screening failure and can be enrolled as a new subject when the UTI is treated, and the subject fulfils the in- and exclusion criteria.

If a subject decides to discontinue prior to day 14 on re-use catheter (day 14 counted from day of Baseline V1), a replacement of the subject must follow. All replacements of subjects must be agreed with sponsor.

6.4. Point of enrolment

A subject is considered enrolled in the investigation when the written informed consent is obtained. The expected duration for each subject is described in Section 5.1 General.

6.5. Subject Identification and Confidentiality

Subjects will be identified in the eCRF and any other document transmitted to the sponsor by the Principal Investigator or delegate, by a unique identification number.

Data entered in the eCRF are confidential and will only be available to the sponsor (including sponsor delegates), members of data management teams, the statistician, members of the EC and if requested to regulatory authorities. The Principal Investigator (PI) will maintain as part of the investigational file a list identifying all subjects entered in the clinical investigation.

7. Procedures

7.1. Clinical investigation-related procedures and assessments

Screening Visit (V0), Week 0:

- Introduction to the investigation and review of Informed Consent Form/Subject Information Form
- Check of in- and exclusion criteria
- Scheduling Baseline Visit (V1) within 3 days unless performed the same day as Screening visit (V0)
- Register the potential subject on the Pre-screening Log if not already registered

Baseline Visit (V1), Week 0: Day 0

- Introduction to the investigation reviewed and confirmed
- Informed Consent signed
- Check of in- and exclusion criteria
- Urine dipstick for hematuria, leucocytes, and nitrite level (Appendix F and G)
- For female subjects of childbearing potential: urine pregnancy dipstick
- Enrolment in the investigation and allocation of subject number
- Collect Baseline information:
  - Gender (male/female)
  - Age (at time of enrolment in years)
  - Height (in cm)
  - Weight (in kg)
  - Reason for using intermittent catheterization
  - When did you start using a catheter? (months/years)
  - Current single use catheter: brand/material/product/item number (at time of enrolment)
  - Single use catheter size at time of enrolment
  - Average number of catheters used per day during the last 1 month
  - Time spent on each catheterization from preparation to storage/disposal (in minutes)

- What is your handedness?
  - Right-handed
  - Left-handed
  - Mixed or cross-dominant (i.e., changes according to task)
  - Ambidextrous (i.e., equal ability in both hands)
- What is your urethral sensation?
  - Normal
  - Impaired
  - Hypersensitive
  - None
- What is your hand dexterity (left/right)?
  - Left hand:
    - Normal dexterity
    - Reduced dexterity
    - Greatly reduced dexterity
    - Don´t know
  - Right hand:
    - Normal dexterity
    - Reduced dexterity
    - Greatly reduced dexterity
    - Don´t know

- Review of concomitant medication at time of enrolment
- Instruct the subject in completing the Baseline questionnaires for evaluation of single use catheter:
  - ISC-Q assessment (paper) (Appendix B)
  - InCaSa assessment (paper) (Appendix C)
  - Perception assessment (paper) (Appendix D)

- Distribution of CLINY Self-Catheterization Set and investigational supplies
- Instruct the subject in use of CLINY accordingly the IFU (Appendix A)
- Instruct the subject in use of weekly urine dipstick form
- Insurance of subjects´ compliance with the CIP
- Scheduling Phone Call Visit (V2) in Week 1, 7 days +/-1 day after Baseline Visit (V1)
- Complete eCRF

Phone Call Visit (V2), Week 1: Day 7 (+/-1 day)

- Review of Adverse events/Serious adverse events/Adverse device events, Device deficiencies and Protocol Deviations
- Review of changes in concomitant medication
- Reminder of instruction for CLINY Self-Catheterization Set
- Evaluation of catheterization since last visit:
  - Have the subject used single use catheters since Baseline Visit
  - Did the subject follow all cleaning procedures stated in the IFU?
  - Average number of daily catheterizations with CLINY the subject completed since Baseline Visit
  - Average time spent on each catheterization from preparation to storage/disposal (in minutes)

- Urine dipstick for hematuria, leucocytes, and nitrite level performed on day of call (weekly urine dipstick form) (Appendix G)
- Remind subject of ending use of CLINY catheter after the test period regardless scheduled date of Visit 5
- Insurance of subjects´ compliance with the CIP
- Scheduling Phone Call Visit (V3) in Week 2, 14 days +/- 1 day after Baseline Visit (V1)
- Complete eCRF

Phone Call Visit (V3), Week 2: Day 14 (+/-1 day)

- Review of Adverse events/Serious adverse events/Adverse device events, Device deficiencies and Protocol Deviations
- Review of changes in concomitant medication
- Reminder of instruction for CLINY Self-Catheterization Set
- Evaluation of catheterization since last visit:
  - Have the subject used single use catheters since last Phone Call Visit
  - Did the subject follow all cleaning procedures stated in the IFU?
  - Average number of daily catheterizations with CLINY the subject completed since Phone Call Visit
  - Average time spent on each catheterization from preparation to storage/disposal (in minutes)

- Urine dipstick for hematuria, leucocytes, and nitrite level performed on day of call (weekly urine dipstick form) (Appendix G)
- Remind subject of ending use of CLINY catheter after the test period regardless scheduled date of Visit 5
- Insurance of subjects´ compliance with the CIP
- Scheduling Phone Call Visit (V4) in Week 3, 21 days +/-1 day after Baseline Visit (V1)
- Complete eCRF

Phone Call Visit (V4), Week 3: day 21 (+/-1 day)

- Review of Adverse events/Serious adverse events/Adverse device events, Device deficiencies and Protocol Deviations
- Review of changes in concomitant medication
- Reminder of instruction for CLINY Self-Catheterization Set
- Evaluation of catheterization since last visit:
  - Have the subject used single use catheters since last Phone Call Visit
  - Did the subject follow all cleaning procedures stated in the IFU?
  - Average number of daily catheterizations with CLINY the subject completed since Phone Call Visit
  - Average time spent on each catheterization from preparation to storage/disposal (in minutes)

- Urine dipstick for hematuria, leucocytes, and nitrite level performed on day of call (weekly urine dipstick form (Appendix G)
- Remind subject of ending use of CLINY catheter after the test period regardless scheduled date of Visit 5
- Insurance of subjects´ compliance with the CIP
- Remind the subject to bring (weekly urine dipstick form) at Termination Visit
- Scheduling Termination Visit (V5) in Week 4, 28 days +/- 3 days after Baseline Visit (V1)
- Complete eCRF

Termination Visit (V5), Week 4: Day 28 (+/3 days)

- Review of Adverse events/Serious adverse events/Adverse device events, device deficiencies and Protocol Deviations
- Review of changes in concomitant medication
- Evaluation of catheterization since last visit:
  - Have the subject used single use catheters since last Phone Call Visit
  - Did the subject follow all cleaning procedures stated in the IFU?
  - Average number of daily catheterizations with CLINY the subject completed since Phone Call Visit

- Average time spent on each catheterization from preparation to storage/disposal (in minutes)

- Instruct the subject in completing the Termination questionnaires for evaluation on the test period with reuse catheter, CLINY Self-Catheterization set:
  - ISC-Q assessment (paper) (Appendix B)
  - InCaSa assessment (paper) (Appendix C)
  - Perception assessment (paper) (Appendix D)

- Preference: (See Appendix E)
  - Catheter preferred (paper)
  - Reason for preference (paper)
  - Consideration to switch to a reusable catheter in the future (paper)

- Reason for drop out if Termination Visit is performed prior to 28 test days
- Urine dipstick for hematuria, leucocytes, and nitrite level (Appendix F & G)
- Review of weekly urine dipstick form for completeness and compliance.
- Ensure of the subjects' wellbeing and compliance with the CIP
- Collect CLINY Self-Catheterization Set. The catheter should be stored in the catheter case WITHOUT Milton solution
- Send CLINY Self-Catheterization set for Laboratory assessments and analysis
- Perform device accountability
- Complete eCRF

7.2. Flow-chart

Table 5: Flow chart showing the connection between visits, assessments, and procedures

	PER-FORMED BY	SCREENING VISIT	BASELINE VISIT	PHONE CALL VISIT	PHONE CALL VISIT	PHONE CALL VISIT	TERMINTION VISIT
VISIT	-	**V0**	**V1**	**V2**	**V3**	**V4**	**V5**
WEEK	-	**WEEK 0**	**WEEK 0**	**WEEK 1**	**WEEK 2**	**WEEK 3**	**WEEK 4**
VISIT WINDOW	-	-	**-3DAYS**	**±1 day 7 DAYS**	**±1 day 14 DAYS**	**±1 day 21 DAYS**	**+3 days 28 DAYS**
GENERAL							
Introduction to the investigation and review of Informed Consent Form/Subjects Information Form	Investigator or delegate	X					
Check of in- and exclusion crite-ria	Investigator or delegate	X	X				
Informed Consent Signed	Investigator and Subject		X				
Allocation of subject number	Investigator or delegate		X				
Collect Baseline information	Investigator or delegate		X				

	PER-FORMED BY	SCREENING VISIT	BASELINE VISIT	PHONE CALL VISIT	PHONE CALL VISIT	PHONE CALL VISIT	TERMINTION VISIT
Review of concomitant medication	Investigator or delegate		X	X	X	X	X
Assess AEs/ADEs/SAEs/SADEs, Device Deficiencies and Protocol Deviations	Investigator or delegate		X	X	X	X	X
QUESTIONNAIRES AND ASSESSMENTS							
ISC-Q assessment	Subject		X				X
InCaSa assessment	Subject		X				X
Perception assessment	Subject		X				X
Evaluation of catheterization since last visit	Subject			X	X	X	X
Preference	Subject						X
Reason for drop out if Termination Visit is performed prior to 28 test days	Subject						X
PROCEDURES							
Urine dipstick for haematuria, leucocytes, and nitrite	Investigator or delegate		X				X
Urine dipstick for hematuria, leucocytes, and nitrite	Subject			X	X	X	
Urine dipstick (female subjects of childbearing potential)			X				
Remind subject of ending use of CLINY catheter after 28 days of use regardless scheduled date of Visit 5	Investigator or delegate			X	X	X	
Reminder of instruction for CLINY Self-Catherization set	Investigator or delegate			X	X	X	
Insurance of subject's compliance with CIP	Investigator or delegate		X	X	X	X	X
Instruct the subject in use of weekly urine dipstick form	Investigator or delegate		X				
Review of weekly urine dipstick form for completeness and compliance							X

	PER-FORMED BY	SCREENING VISIT	BASELINE VISIT	PHONE CALL VISIT	PHONE CALL VISIT	PHONE CALL VISIT	TERMINTION VISIT
Instruct the subject in use of CLINY accordingly the IFU	Investigator or delegate		X				
Distribution of CLINY Self-Catheterization set and investigational supplies	Investigator or delegate		X				
Schedule Baseline Visit (V1) Unless performed the same day as V0	Investigator or delegate	X					
Schedule Visit 2 (Phone Call) 7 days after Visit 1 +/-1 day	Investigator or delegate		X				
Schedule Visit 3 (Phone Call) 14 days after Visit 1 +/-1 day	Investigator or delegate			X			
Schedule Visit 4 (Phone Call) 21 days after Visit 1 +/- 1 day	Investigator or delegate				X		
Schedule Termination Visit V5 (28 days after Visit 1)	Investigator or delegate					X	
Complete eCRF	Investigator or delegate		X	X	X	X	X
Collect CLINY Self-Catheterization set	Investigator or delegate						X
Send CLINY Self-Catheterization set for Laboratory assessments and analysis	Investigator or delegate						X
Perform device accountability	Investigator or delegate		X				X

7.3. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in an electronic CRF (eCRF). Details about data capture can be found in section 11 (Data Management).

CRFs will be completed by the investigator or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log. The delegated site personal will be required to complete e-learning prior to system access. After completed training delegated personal will receive credentials.

It is the responsibility of the investigator that all data, all measurements, and observations are entered promptly and correctly and preferably immediately after the subject has been at site or after a phone call. In case this is not possible the data should be entered no later than 7 days after the visit / procedure.

7.4. Concomitant treatment

Concomitant medication taken from the time of consent through the investigation until termination will be registered in the eCRF in the concomitant section.
Any changes in medicine during the test period must be reported in the concomitant section in the eCRF.
Any kind of antibiotic treatment is not allowed from inclusion through the test period, as this can influence the bacteria type and level investigated on the catheters.

7.5. Supplementary materials and equipment

The investigational device must be used with a lubricating gel, and subjects will be supplied with Optilube, sterile lubricating gel, which is CE-marked. Furthermore, the catheter will be cleansed after use according to the IFU with a Milton cleansing solution (CE-marked), and subjects will be supplied with this as well.

8. Risk – benefit analysis and ethical considerations

8.1. Risk-benefit analysis of the investigational device

A risk analysis according to ISO 14971 Application of risk management to medical devices has been conducted. Risks have been proven minimized or eliminated through appropriate design control, confirmed by pre-clinical bench, laboratory, and clinical testing.

All unacceptable risks related to the device have been mitigated as far as possible and have been deemed acceptable for the clinical study. The CLINY catheter device is already CE marked.

8.2. Risk-benefit for subjects participating in the clinical investigation

The investigation is conducted in accordance with current law and applicable standards. (Section 15, Statement of Compliance), and in accordance with 'The Declaration of Helsinki', 1964, last amended at the 64th WMA General Assembly, Fortaleza, Brazil, October 2013, and ISO 14155 and the Medical Device Directive/Regulation.

The rights, safety and well-being of human subjects shall prevail over the interest of science of society.

The risks in this investigation are considered equal to the use of similar reusable catheters on the market and include haematuria, mechanical trauma, and risks of UTI. Please also see Adverse events, adverse device effects and device deficiencies section 18.

There is no known interaction between the use of the investigational device and the medication participants can take. Disadvantages of testing (trial engagement) may be the time spent on visits, adjustment to new catheter type and routine and responding to questions.

The catheterizations of the subjects with the investigational device will consist solely of self-catheterization, performed by experienced users. Prior to the first catheterization, the users will receive instructions from urology nurses or PI at an investigational site with many years of experience in conducting IC.

There are no direct benefits for the subjects involved. However, potential benefits for the subjects in this investigation may include decreased fear of 'running out', i.e., minimizing the worry about continuous access to catheter. By participating in this investigation, the subjects will contribute with important information with respect to reuse of catheters, and how that practice might influence QoL and catheter hygiene.

8.3. Risk Analysis for the conduct of the clinical investigation

A risk assessment of the clinical investigation will be conducted initially prior to the first subject enrolment and periodically re-assessed based on any new risks identified through the process. This assessment will be completed throughout the duration of the investigation, as defined by the study team. A risk-based monitoring strategy may be implemented including on-site remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

8.4. Delegation of responsibility

Before initiation of the clinical investigation, sponsor must be provided with key site personnel signed and dated curriculum vitae (not more than 2 years old) to verify their qualifications. Key site personnel are those, who treat

or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all site personnel are trained in the investigation procedures, how to complete the case report forms (CRF´s), procedure for reporting an adverse event (AE) or serious adverse event (SAE) or adverse device effects (ADE) or serious adverse device effects SADE) (how, when, to whom), and who to contact in case of emergency related to the investigational device. All training and delegation of tasks will be documented in the Clinical Investigation Training log and the Site Personnel Signature and Delegation log.

9. Monitoring Plan

The sponsor is responsible for ensuring appropriate monitoring of the clinical investigation activities as described below. This study specific monitoring plan includes details regarding the monitoring strategy (i.e., onsite, remote, and centralized).

The monitor will be the primary contact for the PI and delegates.

Monitoring activities are mandatory as per good clinical practice, however the extend and depth of these activities depend on the criticality of the clinical investigation, speed of enrolment, the experience of the clinical investigation personnel in carrying out clinical investigations and specific study designs.

For the purpose of this clinical investigation the below described monitoring procedures have been selected.

The data collected throughout the investigation and the conduct of the investigation, will be monitored per the monitoring plan to ensure, and verify, that the rights and well-being of the subjects are protected, that the reported data are accurate, complete, and verifiable from source documents, and that the conduct of the investigation complies with the approved CIP, subsequent amendment(s), ISO14155 and the applicable regulatory requirement(s).

The monitoring process is described below.
The monitoring in this investigation will be conducted periodically at all sites by the Clinical Manager.

The investigator must be available for and agrees to cooperate with Coloplast Clinical Managers (CM) during their visits and ensure that they have direct access to all documents that they require, including direct access to the subject's files.

The investigation will be subject to internal audits if relevant. All monitoring visits and possible audits will be followed by internal reports and corrective actions, if needed.
Follow-up letters will be forwarded to sites after all visits and any findings should be addressed by the investigator or delegate.

To ensure proper conduct of the investigation the following visits on site will be performed before/during the investigation:

- Site selection visit
- Site initiaton visit
- Periodic monitoring visits
- Close out visits

9.1.1. Site selection visit

Depending on the prospective clinical investigation and sites experience with the specific investigational device, an on-site qualification or site selection visit shall be performed during which the feasibility of the clinical investigation requirements will be discussed. A common agreement between sponsor and Principal Investigator shall be reached. This visit may also be replaced by one or more phone calls or remotely, using Microsoft Teams, Skype, or Face Time, if the Principal Investigator is known to the sponsor or if the site is restricting visitors due to the Covid-19 pandemic.

9.1.2. Initiation visit

An initiation visit with full training on all aspects of the clinical investigation will be provided.
The initiation visit will be held as a physical meeting or remotely using Microsoft Teams, Skype or Face time and the visit will be held as close to study start as possible.

Before initiation of the clinical investigation, sponsor must be provided with key personnel signed and dated curriculum vitae (not more than two years old) and documentation of current ISO14155 training (within the last two years) to verify their qualifications.

All clinical investigation sites will complete an initiation visit during which full training on all aspects of the clinical investigation will be provided including training in handling of the investigational test product, the CLINY Self-Catheterization Set. This visit can also be conducted on-site or remotely if the site is restricted visitors due to the Covid-19 pandemic.

9.1.3. Monitoring visits

The sponsor shall determine the extent and nature of monitoring appropriate for the clinical investigation based on the risk assessment. The sponsor shall ensure, through oversight of the clinical investigation and timely adverse event reporting, that unanticipated adverse device effects are identified and investigated rapidly so that, where necessary, additional risk control measures can be implemented.

The monitor is to ensure adherence to the clinical investigation plan, the safety of the subjects, accurate data recording on the e-CRFs and to monitor recruitment rates and adherence to follow-up schedules. During the clinical investigation, monitors shall check that appropriate written informed consents have been obtained. The Principal investigator shall permit and assist the monitor to carry out verification of completed eCRFs against data in the source documents.

The Principal Investigator can delegate tasks to his/her collaborators, however the roles and responsibilities as time of involvement for each clinical site personnel must be documented on the Site Personnel signature and Delegation list as well as training received before getting involved with the clinical investigation must be documented in the Clinical Investigation Training Log.

The monitor shall inform the sponsor about any problems relating to facilities, technical equipment, or medical staff at the clinical investigation site. The monitor shall also be responsible for notifying such deficiencies in writing to the Principal Investigator and convene with the clinical investigation site personnel appropriate and timely corrective actions.

The sponsor, or delegate, will provide clinical monitoring, including review of eCRF with verification to the source documentation, as defined later in this monitoring plan.

Before doing any review of subject data, the monitor must review the signed Informed Consent Forms and only monitor data from subjects with a correct signature on these forms. The monitor shall also be responsible for notifying such deficiencies in writing to the investigator and convene with the clinical investigation site personnel appropriate and timely corrective actions.

The first monitoring visit at the site should be conducted as soon as reasonably possible after the first subject(s) has(have) completed the first visit of the investigation. This is to minimise systematic errors done by site and to clarify potential questions before proceeding with enrolment of more subjects.

Additional monitoring will be conducted in accordance with the recruitment rate or if there is a need for more frequent visits upon request from site or Clinical Manager.

The Investigation Site File shall be monitored for 100% completion per the Investigation File Requirement Checklist. Monitoring activities will be documented in a site visit report. A follow up summary describing the observations, including documentation of any deviations and actions required shall be provided as soon as reasonably possible to the Principal Investigator and/or delegate after the conducted monitoring visit.

All data collected can be directly entered in the eCRF. The monitor will by edit checks ensure that all fields are completed in the eCRF. Monitor will ensure by closely monitoring, that all queries are timely resolved.

The sponsor representative (Clinical Manager) will have close contact to the site in the recruitment period to ensure that any concerns, problems, or recruitment challenges are solved with the site in a timely manner.

Only the Principal Investigator, delegated site personnel and the sponsor representatives will have access to all the eCRF records.

9.2. Source data verification

Source data is all information in original records, certified copies of original records of clinical findings, observations, or other activities in the clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. This includes source data initially recorded in an electronic format. A source document is a document in which data collected for a clinical investigation is first recorded.

All documents and data related to the clinical investigation handled by site personnel, shall be produced, and maintained in a way that assures reliability, integrity, control, and traceability, and shall be appropriately stored to provide a complete history.

The Principal Investigator shall assure the accuracy, attribution, completeness, legibility, and timelines of the data reported to the sponsor in the eCRFs and in all required reports. All printed copies of electronic source documents shall be certified, as indicated by a dated signature by the investigational site personnel at the time the document is printed. Special requirements should be applied to the capture, review, and retention of electronic source data, to ensure reliability, quality, integrity, and traceability.

The data reported in the eCRF shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. The eCRF can serve as the source document and this must be documented on the Source Data Specification Form. The Source Data Specification Form must be completed at the initiation visit detailing the location of the source data for each data point agreed upon by the Principal Investigator.

Data points for data verification:

- Infomed Consent Form
- In- / Exclusion criteria
- AE/ADE/SAE/SADE/DD
- Other

Written informed consent, in- and exclusion criteria and all AE´s, ADE´s, SAE´s, SADE´s and DD occurring in the investigation will be 100% verified for timely completion for all subjects enrolled in the investigation.

9.3. Remote monitoring

Remote or centralized monitoring is a remote evaluation carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than the site(s) at which the clinical investigations is being conducted. Remote monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

In addition to onsite monitoring visits, remote monitoring of the data entered in the eCRF system could be used to achieve the following:

- Conduct activities such as: standard checks of range, consistency, and completeness of data and checks for unusual distribution of data, such as to little variance.
- Special attention will be given in case of frequent data anomalies or errors, protocol deviations/violations or excessive dropouts.
- Augment on-site monitoring by performing monitoring activities that can only be accomplished using centralized processes (e.g., statistical analyses to identify data trends not easily detected by on-site monitoring).
- Monitor data quality through routine review of submitted data in real-time to identify missing data, inconsistent data, data outliers, and potential protocol deviations that may be indictive of systemic and/or significant errors in data collection and reporting at the site.
- Verify source data remotely, provided that both source data and eCRF´s can be assessed remotely.

- Conduct aggregate statistical analyses of the study data for plausibility and completeness.
- Conduct analyses of site characteristics, performance metrics (e.g., high screen failure rates, high frequency of eligibility violations, and delays in reporting data), and clinical data to identify early on corrective actions needed for characteristics correlated with poor performance or noncompliance.

10. Statistical considerations

10.1. Statistical design, method, and analytical procedures

Baseline assessments and endpoints will be reported by descriptive statistics and/or listed. Summaries will be presented by device i.e., IC and re-use catheters and if relevant, by other grouping variables.

Descriptive statistics for continuous variables are presented with N, Mean, SD (standard deviation), Median, Min and Max, where N denotes the number of subjects contributing with non-missing data. For discrete variables, descriptive statistics are presented with N and percentage, where percentage is based on the total number of subjects/observations with non-missing data.

All statistical analysis will be performed with [redacted]

10.2. Definition of analysis populations

Screening Failures (SF), Intention to Treat (ITT), Full Analysis Set (FAS) and Safety populations will be defined at a formal data review meeting prior to database lock. As a minimum, the data management specialist, the clinical manager, and the statistician will be involved in the classification of subjects.

Subjects not adhering to inclusion and/or exclusion criteria are considered screening failures (SF).

The Safety population will constitute all subjects enrolled i.e., subjects who have given informed consent.

The full analysis set is a modified ITT population i.e., a sub-population of the ITT population, and will constitute all subjects enrolled, who have been exposed to at least one device, with at least one endpoint recorded (data non-missing).

Individual endpoints/data points may be excluded from the analysis, even though the corresponding subject belongs to any of the pre-defined populations. Exclusion of subjects or data points must be documented.

All statistical analysis will be based on the full analysis set, whereas adverse events and device deficiencies will be assessed in the safety population.

10.3. Analysis of the primary endpoint

HR-QoL index score will be analysed in mixed model with subject included as a random component and catheter (IC and re-use catheters) included as a systematic effect.

Evidence of significant effect will be concluded, if the 95% confidence interval of the difference between IC and re-use catheters, do not include zero.

10.4. Analysis of the secondary and exploratory endpoints

Adverse events and exploratory endpoints will be reported end evaluated by descriptive statistics.

10.5. Sample size

As this is an exploratory study no formal sample size calculation has been performed.

In a previous publication[14] results of effect were seen with 37 completers. Hence, we aim for 40 male or female IC users in this study.

Discontinued subjects will be asked for completion of Termination Visit (V5), where the subjects will be asked to state their reason for terminating the study.

If a subject decides to discontinue prior to day 14 on re-use catheter (day 14 counted from day of Baseline V1), a replacement of the subject must follow. All replacements of subjects must be agreed with sponsor.

10.6. Level of significance and power

A significance level of alpha 0.05 (2-sided) will be applied.

10.7. Pass/fail criteria

Due to the exploratory nature of this investigation, no formal pass/fail criteria are applied. A positive as well as a negative outcome of any endpoint will provide knowledge that is useful in the further decision-making and development.

11. Data management

11.1. Data Collection in the clinical investigation

Data management and the final statistical analyses of all measurements described in this protocol are carried out by [redacted] Coloplast A/S.

Data will be collected through an electronic data capturing (EDC) system on electronic Case Report Form (eCRF), a secure, internet-based case report form. This system will be used to record all subject information collected in the investigation for secure data tracking and centralised data monitoring ("remote monitoring") done by monitors, as defined in the monitoring plan.

The EDC system used is [redacted] delivered by [redacted] The system is designed to be compliant with the FDA requirements of 21 CFR part 11. It is a validated data management system allowing only qualified and trained personnel to enter the system. The system has full audit trail and electronic signature.

The sponsor will be responsible for training the investigator or delegate, in completion of the eCRF.

Principal Investigator, or delegate, at the clinical site will perform primary data collection directly into the eCRF or drawn from source-document reviews. The eCRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up.

The eCRF will be completed by the investigator, or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log. It will be the responsibility of the investigator to ensure that all measurements and observations are correctly noted in the eCRF.

All assessments and observations throughout the investigation for each subject must be carefully recorded in an eCRF or in a paper CRF (pCRF) during the visit or immediately after. The eCRF makes it possible to enter data right away when they are obtained. This is the preferred way of collecting data. In case this is not possible the data should be entered no later than 7 days after the visit / procedure.

Subject reported outcomes (The HR-QoL questionnaire (ISC-Q), InCaSa questionnaire, Perception Questionnaire, Preference, reason for Preference and subject dipstick diary) will be completed by the subject in paper CRF and entered in the eCRF by the site personnel.

Data from the lab analysis will be batch uploaded into the EDC system. Adverse events should be registered following the timelines described in the Adverse Event section. In the unforeseen situation, where site cannot establish connection to the EDC system a paper CRF (pCRF) has been printed and supplied by sponsor.

The investigator will keep a separate list of the subjects' ID numbers, names and addresses in a locked room/cabinet. Only data referred to in this clinical investigation plan will be recorded in the CRFs.

11.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The principal investigator and delegate(s) must be trained in the system prior to getting access. The training is web-based and must be completed before

access to the investigation is granted. Training will be documented in the data management system. Only the principal investigator, or delegate, will be authorised to enter data in the eCRF.

The monitor, using his/her personal login information shall verify all critical data points against the source documents and issue electronic queries for the authorised clinical site personnel to respond, as defined in the monitoring plan.

The principal investigator, using his/her personal login information shall sign each eCRF.
Automated, real time access to the data enable control on study compliance and safety assessments.

A critical quality control will be performed by the sponsor's data management team and queries issued where needed. Such queries will be reviewed by the monitor and must be resolved by the site personnel.

At the end of the study a formal data review meeting will be performed before the database will be locked.

A full audit trail ensures, that each user's (site personnel, monitor, sponsor, data manager) access to and actions in the system is tracked.

The Data Management Procedures are further described in the Data Management SOPs.

11.3. Data retention

The Investigator file must be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

12. Amendments to the Clinical Investigation Plan

No changes in the clinical investigation procedures shall be affected without mutual agreement between the principal investigator and the sponsor. The agreement of the changes must be documented by signing the cor-responding clinical investigation plan amendments and registered in the Change Log.

All significant changes require notification to the EC and applicable regulatory authority. Substantial changes may require approval from the EC and applicable regulatory authority prior to implementation.

13. Deviations from the Clinical Investigation Plan

Deviations to the Clinical Investigation Plan occurs when the activities during the clinical investigation do not comply with the EC approved investigation plan.

A minor deviation is defined as those that does not increase risk or decrease benefit or don't have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data. If a deviation increases risk or decreases benefit and/or has a significant effect on the subject's rights, safety, or welfare and/or has a significant effect on the integrity of the data it is defined as a major deviation and the Investigator must inform the monitor immediately, and the monitor will report and inform the Clinical Manager or designee immediately. For this investigation, the Clinical Manager must be informed immediately by the Investigator.

The investigator is not allowed to deviate from the Clinical Investigation Plan unless, under emergency circumstances or to protect the rights, safety, and welfare of the subject(s).

For the purposes of this investigation, any variance from the protocol is considered a deviation and is to be reported.

The site will complete a deviation eCRF form for all data-related deviations and all deviations that are **not** related to the data (*for example, an untrained nurse performing study procedures*) are reported by the monitor in the Site Report – Periodic Monitoring and actions are addressed to the Investigator for completion.

If any deviations to the Clinical Investigation Plan are detected during the monitoring visit, the monitor shall ensure the site reports all deviations in the eCRF or on the Deviation log in the Investigator File. Additionally, the monitor must report any deviation noted during the visit in the Periodic Monitoring Report.

Monitor will align with data management in each investigation, how data management will be informed about all deviations.

Details about the deviation will be collected, for example:

- Site ID, Subject ID
- Deviation Date
- Date deviation was discovered
- Clear and concise description of the event
- What the deviation is related to
- Provide a reason and record the corrective action taken, including the date of the corrective action. Please note corrective action can be site was re-educated on a procedure. Ensure the corrective action is documented.
- Record the EC notification date, when applicable, and retrieve a copy of the EC Submission Letter for the TMF.

14. Device Accountability

All access to the investigational devices used in the clinical investigation is controlled by storage procedures and device accountability logs as described below. The investigational devices must only be used in this clinical investigation and only according to the Clinical Investigation Plan.

Sponsor keeps a device accountability log that states the physical location of all investigational devices from shipment of investigations devices to the investigational sites until return of or disposal.

The Principal Investigator or an authorized designee keeps records documenting the receipt, use and return and disposal of the investigational devices, which includes:

- Name of the product received
- Date of receipt
- Identification of each investigational product (item no./lot no)
- Number of products received
- Number of products distributed to subjects
- The expire date
- The date(s) of use
- Subject identification
- The date on which the investigational device was returned/explanted from the subject
- The date of return unused, expired or malfunctioning investigational devices or products to Sponsor

For this investigation, all returned CLINY Self-Catheterization sets to sponsor for further analysis and laboratory assessments must be documented on the device accountability with date of return.

15. Statement of compliance

The clinical investigation is conducted in accordance with:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 64th WMA General Assembly, Brazil, October 2013.

- MDD 93/42/EEC as amended by Directive 2007/47/EC (commonly known as the Medical Device Directive).
- MDR (EU) 2017/745
- ISO 14155:2020 "Clinical Investigation of medical devices for human subjects – Good clinical practices".
- The EU General Data Protection Regulation (2016/679)
- Any applicable regional or national regulations will be specified in the country specific CIP.

15.1. Ethics committee and regulatory authorities

The Clinical Investigation Plan and/or other relevant documents are submitted to the appropriate EC(s). This clinical investigation will not begin until the required approval from the EC(s) has been obtained. Any amend-ment to the protocol will be submitted to the same EC(s).

Sponsor will notify the EC(s) concerned of the end of the clinical investigation.

15.2. Data protection

As part of the investigation Coloplast A/S, Holtedam 1, 3050 Humlebaek, Denmark ("Coloplast") will collect and process the personal information the subject provides for the investigation ("subject personal data"). This includes identification and contact information (which may be anonymised depending on the nature of the investigation) as well as information about product usage experience and your health. Coloplast will comply with the EU General Data Protection Regulation (GDPR) and the Danish act on data protection ("databeskyttelsesloven"), including in connection with transfer of data to third countries, cf. chapter V of GDPR, Coloplast will only process the subjects' personal data:

1. To conduct the investigation and carry out related research based on subject consent (primary use), cf. articles 6(1)(a) and 9(2)(a) of GDPR,
2. To comply with applicable legal obligations to e.g., ensure reliability and safety, cf. article 6(1)(c) in conjunction with article 9(1)(i) of GDPR, and
3. If separate consent is given for secondary use of subject personal data, cf. articles 6(1)(a) and 9(2)(a) of GDPR – carry out research outside the clinical protocol to improve Coloplast's products and services, and for use in education.

Part of Coloplast's processing is carried out on third-party platforms (clinical trial databases) and certain third parties are assisting Coloplast in the processing (e.g., the investigator). Such cases will imply a transfer of your personal data to the third parties, but solely for the specified purposes and with the third parties acting on instruction from Coloplast. Data may be collected and processed across the Coloplast network, which may entail processing of personal data outside the European Economic Area. In such cases, an adequate level of protection will be ensured by the third parties being subject to the standard contractual clauses on data protection adopted by the EU or to an EU-approved certification mechanism on data protection. For further information about this please the subject can always consult Coloplast's data protection officer (details below).

Subject personal data will be kept as long as required under applicable laws and regulations. The EU Medical Device Regulation obligates Coloplast to keep the data for a period of at least ten years after the investigation is completed, or, if the device is subsequently placed on the market, at least ten years after the last device has been placed on the market. Subject personal data will be deleted at the end of the mandatory retention period.

If the subject has questions or queries regarding Coloplast's handling of personal information, the subject can always contact Coloplast's Data Protection Officer at [redacted] Complaints related to Coloplast's handling of subject personal information may similarly be sent to the Data Protection Officer, and the subject is also entitled to file a complaint with the relevant supervisory authority, which in the case of Denmark is the Danish Data Protection Agency (www.datatilsynet.dk).

The subject can write to [redacted] at any time to request:

- Access to personal data

- Correction of errors in personal data or to erase personal data
- Limit what can be done with personal data
- To receive personal data in machine-readable format (data portability).
- Withdrawal of consents the subject has given Coloplast to process personal data

15.3. Indemnity

All subjects are fully covered by Coloplast A/S insurance throughout the investigation.

Insurance has been signed with:

[redacted]

15.4. Financial conditions

Coloplast A/S will compensate all investigators involved in the clinical investigation for their time and resources spent on the investigation. All financial agreements with the investigation sites involved in the clinical investigation will be specified in a sponsor investigator agreement.

The expenses include the salary to the Principal Investigator, the cost of external clinical support, study supplies, eCRF, Investigator and site personnel training and patient expenses including travel expenses.

The Principal Investigator and site personnel have no financial interests in the investigation.

The total budget for the investigation is [redacted] covering 40 participants. The expenses are paid on an ongoing basis.

16. Informed consent process

Written informed consent is obtained from all subjects participating in the investigation after thorough written and verbal information. The information is given by the investigator or his/her representative in the subjects' native non-technical language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks, or inconveniences and/or expected benefits, all anticipated adverse device effects and then have a minimum of 24h before deciding on participation. The subjects will be informed that their participation is voluntary and that they may leave the investigation at any time, without this having any influence on their further treatment.

The informed consent signature form includes personally dated signatures of the subject and the PI or his/her representative responsible for conducting the informed consent process. A copy will be provided to the subject.

If new information is to be given during the investigation, sponsor will inform the investigators, and the new information is given to the subjects by the investigator. If new information becomes available that can significantly affect a subject's future health and medical care, that information will be provided to the subject in written form. The Clinical Manager is responsible for writing the information and providing the approved Informed Consent Form/Subject Information Form to investigators that will further provide it to the subjects.
If applicable, all affected subjects shall be asked to confirm their continuing informed consent in writing.

17. Subject compensation

17.1. Compensation in case of injury

Device liability and No-Fault Clinical Investigation Insurance covering the duration of the clinical investigation are in place, to enable compensation in the event of an injury to a participating subject

17.2. Compensation for participating in the clinical investigation

Subjects will be compensated with a voucher per visit, paid by Coloplast A/S with the value as described below:

	Subjects
[redacted]	

This is to compensate for any inconvenience caused during the catheterisations and time used on site visits.

There are no medical benefits for the subjects participating in the investigation, however participation will contribute to important knowledge on catheters and be in favour of the aim of the investigation.

Each voucher will be handed to the subject after a completed visit. Withdrawn subjects will not, for any reason, be compensated with vouchers for uncompleted visits.

Travel expenses will be accounted for separately. The remuneration/vouchers are taxable (B-income) and it is the responsibility of the subject to declare this to SKAT.

The subjects will not be compensated for the loss of earnings during their participation.

18. Adverse events, adverse device effects and device deficiencies

18.1. Adverse events

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, whether or not related to the investigational medical de-vice(s) or the comparator(s), or the procedures involved. The adverse event shall be marked with the intensity mild, moderate, or severe. This could include events such as headache or dizziness.

18.2. Adverse device effect

An adverse event, which is related to the use of the investigational medical device, is an adverse device effect, and should be marked as unlikely related, possible related, probable related or with causal relationship on the adverse event form.

The definition of an adverse device effect includes any event resulting from insufficiencies or inadequacies in the instruction for use, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device. Table 6 lists anticipated adverse device effects that may occur.

Table 6: Anticipated adverse device effects and their likely incidence rates

ANTICIPATED ADE	INCIDENCE RATE
Urinary tract infection	Unlikely
Macroscopic haematuria	Unlikely
Stinging and pain in urethra during catherization	Likely
Irritation of mucosa	Likely

18.3. Device deficiency

A device deficiency is the inadequacy of the investigational medical device or comparator with respect to its identity, quality, durability, reliability, usability, safety, or performance. This includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labelling.

18.4. Serious adverse events (SAE)

A serious adverse event is an adverse event that:

- Led to death,
- Led to a serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
  1) a life-threatening illness or injury, or
  2) a permanent impairment of a body structure or a body function including chronic diseases, or
  3) in-patient or prolonged hospitalization, or
  4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Led to foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment.

This includes device deficiencies that might have led to a serious adverse event if:

- Suitable action had not been taken, or
- Intervention had not been made, or
- Circumstances had been less fortunate.

These are handled under the serious adverse event reporting.

Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

18.4.1. Serious adverse device effect (SADE)

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

18.4.2. Unanticipated serious adverse device effect (USADE)

An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report.

18.5. Medical care of subjects

The Principal Investigator shall ensure that adequate medical care is provided, during and after participation in the clinical investigation, to a subject experiencing an adverse event. All ongoing ADEs, SAEs, SADEs and DDs that could have led to a SAE at subject termination will be followed according to the Risk Benefit analysis (see section 8). An ongoing adverse event at subject termination visit is documented as the current status for the adverse event and will not be followed up.

The subjects shall be informed of any new significant findings occurring during the clinical investigation, including the need for additional medical care that can be required, and of the nature and possible cause of any adverse events experienced.

Principal Investigator shall provide the subject with the necessary instructions on proper use, handling, storage and return of the investigational device when it is used or operated by the subject.

18.6. Reporting and timelines

18.7. Investigator's reporting responsibilities

- PI at each site must assess all (S)AE`s that occur at his/her site.
- All serious adverse events and serious adverse device effects must be reported to sponsor within 24 hours of the site becoming aware of the event.

- A device deficiency that could have led to a serious adverse event but did not because suitable action was taken, intervention had been made or because of fortunate circumstances should be reported to sponsor within 24 hours of the site becoming aware of the event.
- New findings and/or updates in relation to already reported serious events should also be reported to sponsor within 24 hours of the site becoming aware of the event.
- Device deficiencies and all adverse device effects related to CE marked investigational product and/or comparator must be reported to sponsor within 24 hours of becoming aware of the event.

When reporting the SAE, the relationship to the test material shall be described whether the event is considered

- **Not related**, the event has no temporal relationship with the use of the test material or the procedures.
- **Unlikely related,** the relationship with the use of the test material seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible related,** the relationship with the use of the test material is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
- **Probable related,** the relationship with the use of the test material seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- **Definitely related/Causal relationship,** the event has a temporal relationship with the test material use/application or procedures.

and the intensity of the event should be considered, as such:

- **Mild,** the intensity of the event is mild with no further action or intervention
- **Moderate,** the intensity of the event will lead to an action or intervention to solve the event
- **Severe,** the intensity of the event will lead to follow up on the action or intervention, as the effect of the action or intervention may not decrease the symptoms.

All above events must be reported by use of the relevant adverse event/serious adverse event/device deficiency form.

Please report to: [redacted] In cases where assessing the e-mail is not possible, please call [redacted]

18.8. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported *to Danish regulatory authorities* immediately, but no later than 7 calendar days following the date of awareness by sponsor.

- All serious adverse events
- All serious device effects
- All device deficiencies that could have led to serious adverse events but did not because suitable action was taken, intervention had been made or because of fortunate circumstances.
- New findings and/or updates in relation to already reported events.

If the serious adverse event results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action for other subjects, users or other persons or a new finding to such a serious adverse event, sponsor must immediately but no later than 2 calendar days after awareness by sponsor report the event to Danish regulatory authorities and ethics committees, as applicable.

It is the responsibility of sponsor to inform all investigators in writing within 10 working days if device deficiencies, adverse events, adverse device effects, near-incidents, serious adverse events, serious adverse device effects or unanticipated serious adverse device effects lead to corrective actions.

19. Suspension or premature termination of the clinical investigation

Sponsor may suspend or prematurely terminate an investigation site or the entire clinical investigation for documented significant reasons.

If a suspicion of an unacceptable risk to subjects develops during the clinical investigation, sponsor will suspend the investigation while the risk is assessed. Sponsor will terminate the investigation if an unacceptable risk is confirmed. Sponsor will ensure that the premature termination will be justified in writing and will promptly inform the regulatory authorities and Ethics Committee.

If monitoring or auditing of the clinical investigation identifies serious or repeated deviations at one of the participating investigation sites, sponsor will suspend or terminate the particular investigational site. The sponsor or investigator will inform the regulatory authority as appropriate and notify Ethic Committee about the termination of the site.

20. Clinical investigation report

At completion of the Clinical Investigation, Sponsor is responsible for writing the clinical investigation report. The report is retained on file. The report contains a critical evaluation of all data, which have been collected during the investigation. The report describes the methodology and design and a data analysis, including statistical preparation and conclusion.

Sponsor and national coordinating investigator must sign the final version of the clinical investigation report or an affidavit, indicating their agreement with the contents. If no coordinating investigator is appointed, then the signatures of the principal investigators should be obtained.

The clinical investigation report must be submitted to Ethic Committee within a year of the termination of the clinical investigation.

21. Publication policy

Coloplast, the sponsor, is referring to the internal document "Clinical Publication policy" that will be available for internal and external persons involved in the publication process.

The investigation will be registered on a public accessible database www.ClinicalTrial.gov, before recruitment of the first patient.

The results of the investigation, positive as well as negative, may be communicated by abstracts, posters, or oral presentations provided that opportunity is given for sponsor to discuss the contents and any conclusions drawn, before the abstract, paper, or visual presentations are finalised. In all cases the subject's identity will remain confidential.

Sponsor will undertake to comment on the draft documents within 30 working days of receipt, but the final decision on the contents and format of the publication from the conclusions drawn, will remain with the authors.

No preliminary results will be published.

Data from the investigation is considered confidential until it is published according to the conditions of this Clinical Investigation Plan.

Sponsor may publish single subject case stories at any time during and after the investigation.

Sponsor reserves the right to use the data (published or unpublished) for reimbursement or regulatory purposes.

21.1. Joint publication (multicentre investigation)

A joint paper will not be published before all PIs have approved the content of the clinical investigation report. If a site cannot approve the results/conclusions drawn, an independent Ethic Committee will be asked to review, and all investigators must follow its conclusion.

Decisions regarding authorship credit will follow the "Uniform Requirements for Manuscripts submitted to Biomedical Journals" (the Vancouver group) according to which an author of a publication must fulfil the following criteria:

- Substantial contribution to conception and design, or acquisition of data, or analysis and interpretation of data.
- Drafting the article or revising it critically for important intellectual content.
- Final approval of the version to be published.

Investigators who do not meet all the above criteria for authorship will be listed in the acknowledgment section under the heading "clinical investigators" and their function or contribution described. All persons must give written permission to be acknowledged.

21.2. Individual publication (multicentre investigation)

Individual sites may only publish their own data from the investigation (case histories not included) in the case that:

- No joint publication is planned, or a joint paper has already been published.
- Approval from sponsor and/or the PI has been obtained.

22. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if

- major non-adherence to the clinical investigation plan is occurring
- it is anticipated that the subject recruitment will not be adequate to meet the investigation objectives at least 75% of the subjects should be entered within the recruitment time.

In case sponsor withdraws, sponsorship for the subjects already recruited into the clinical investigation will continue.

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Appendix A: IFU – CLINY Self-Catheterization Set

Self-Catheterization Set

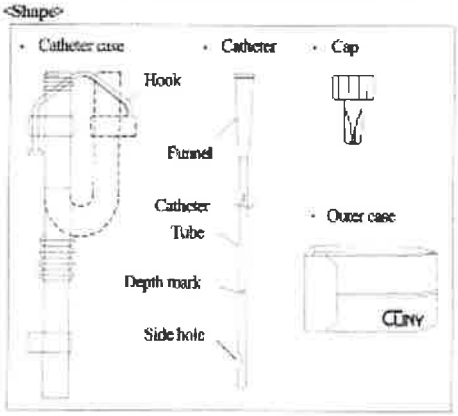
Instructions for use

[Warning]
This device must be used after it has been disinfected using an appropriate disinfectant of right concentration.
[It is a non-sterilized product.]

[Contraindications / Prohibitions]
- Do not sterilize this device except disinfectant.
- Do not resort to sterilization and/or boiling to the catheter case, cap and outer case
  [Otherwise, it may deform the device and impair the intended function.]

[Shape, Structure, and Brief Description on the Usage, etc.]

<Shape>



<Material>
- Catheter case : Polypropylene , Silicone rubber
- Cap : Polypropylene, Silicone rubber
- Catheter : Silicone Rubber

<Specifications>

	Catheter			
	Size	Outer diameter	Total Length	Feature
Female Type	10Fr	3.3mm	165mm	1 side hole
	12Fr	4.0mm		
	14Fr	4.7mm		
	16Fr	5.3mm		
Male Type	10Fr	3.3mm	300mm	1 side hole
	12Fr	4.0mm		
	14Fr	4.7mm		
	16Fr	5.3mm		
Male L. Type	12Fr	4.0mm	350mm	1 side hole
	14Fr	4.7mm	385mm	2 side holes
Tiernan Type	12Fr	4.0mm	300mm	1 side hole
	14Fr	4.7mm		
CUR Type	14Fr	4.7mm	395mm	5 side holes
	16Fr	5.3mm		
	18Fr	6.0mm		
	20Fr	6.7mm		

	Catheter		Outer case
	Size	Depth mark	Measurement
Female Type	10Fr	Depth marks in 10mm intervals from the tip to the positions indicating 10 to 100mm.	60×117×15mm
	12Fr		
	14Fr		
	16Fr		
Male Type	10Fr	Depth marks in 10mm intervals from the tip to the positions indicating 50 to 200mm	60×190×15mm
	12Fr		
	14Fr		
	16Fr		
Male L. Type	12Fr	Depth marks in 10mm intervals from the tip to the positions indicating 50 to 200mm.	60×232×15mm
	14Fr	Depth marks in 10mm intervals from the tip to the positions indicating 100 to 250mm.	
Tiernan Type	12Fr	Depth marks in 10mm intervals from the tip to the positions indicating 50 to 200mm.	60×190×15mm
	14Fr		
CUR Type	14Fr	Depth marks in 10mm intervals from the tip to the positions indicating 100 to 250mm.	60×232×15mm
	16Fr		
	18Fr		
	20Fr		

<Principals>
Put the catheter in the catheter case filled with disinfectant.
In case of carrying, it is possible to bend the catheter with catheter case concurrently.

[Intended Usage, Indications and Effect]
The device is to be inserted temporally into the patient's urethra, bladder, ureter, or drainage port after urinary diversion surgery to be used for urination.

[Specification of Component]
The catheter can endure the pull strength from the both ends at the load of 4.9 N without tear.

[Operation Procedure]
A typical operation procedure is described below;

1) Straighten the catheter case and fill the catheter case with a disinfectant of right concentration. See the following drawing as target amount of solution (Figure 1).

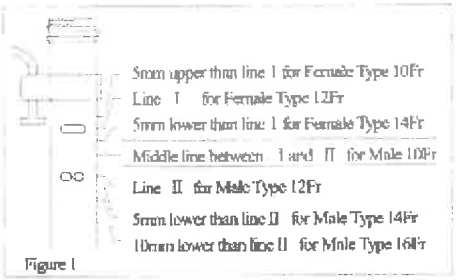


Figure 1

2) Push the cap into the funnel until the chase of the cap places at the second lib of the funnel in order to fix firmly. (Figure 2).

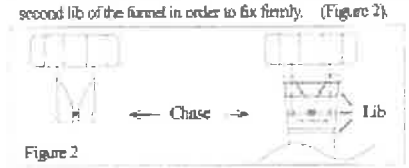


Figure 2

3) Straighten the catheter case and insert the catheter with cap into the catheter case. Turn the cap surely and lock it in firmly. And make sure that disinfectant is not leaked from the catheter case.
4) Pull out the catheter and take urination procedure.
5) After use, clean the catheter with tap water, boiling and so on. And then house and store it into the catheter case filled by disinfectant according to the steps 2) to 3) of [Operation Procedure].
6) After bending the catheter case and keep the bended form by hook, put it in the outer case.

<Precautions related to the operation procedure>
When place the funnel into the cap, push the funnel to specific position (See figure 2).
After screw the cap, make sure the catheter case and the cap fit completely, and disinfectant does not leak from the case.
[Leakage of disinfectant may occur]

[Precautions]
<Important general instructions>
1) In case of not use this device for long time, do not bend the catheter case. Straighten the catheter case when it stores.
2) Prescribe an appropriate disinfectant of right concentration for the patient. Below provides the drug name and the reference concentration for use, for information. However, the concentration must be decided considering the patient conditions based on the physician's experiences.

General name	Reference concentration for use	Usage experience
sodium hypochlorite	0.0125~0.02%	Dilute "Mihon" 50 to 80 times with water

Generic name	Reference concentration for use
Benzalkonium chloride solution	0.05 - 0.1%
Benzethonium chloride solution	0.05 - 0.1%

Note) The device may be colored depending on the disinfectant used.
3) Before using this product, check every component for any abnormalities.
4) Do not insert the catheter forcibly. If there is difficulty in insertion, stop the use and take appropriate measure.
[Otherwise, it may harm the patient's tissues.]
5) Avoid forcible insertion or removal, and operate with a good care.
[Otherwise, it may cause breakage of the device.]
6) If there is any abnormality, stop the use immediately and take appropriate measures.
7) If upon use of the device, do not pull or bend it forcibly. Handle it gently and carefully.
8) Do not modify the product.
[If any feature (e.g. side hole(s)) is added, it may cause breakage of the catheter.]
9) Do not expose this product to an organic solvent, strong acid, strong base, or any equivalent agent.
10) Do not hold this product strongly with forceps or other tool.
[Otherwise, it may cause a tear of the catheter or clogging in the lumen.]
11) In case of any abnormality including damage in the package or the device, do not use the product.
When (STERILE) is found on the label, it means that the product should not be used if the package has been damaged or opened.
12) After opening, use the device appropriately. After replaced to a new device, the obsolete device should be disposed in a safe manner.
13) When (DEHP) is found on the label, it means the product doesn't contain DEHP in the contact part with body fluid and drug solution.

<Adverse events>
- Urethralgia or distress during catheter insertion at initial period of self-catheterization.
- Urinary tract infection such as cystitis or pyelonephritis.
[In the case of having a small urinary volume every day or a difficulty in keeping herself/himself clean.]
- False passage (In case of male)
[Forcible catheter insertion]
- Leakage of disinfectant.

[Method of Storage and Shelf Life]
<Method of storage>
This product must be stored under clean conditions and prevented from direct sunlight, high temperature and humidity, low temperature below 10℃, and ultraviolet ray including a sterilamp.

<Usable period>
This product is recommended to be replaced with a new device within 1 month.

<Shelf life>
- Follow the proper storage methods, and use the use before date printed on the each package.
- Store the product with great care, and do not use the device if it passed the use before date.

[Packaging]
5 sets /box.

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Appendix B: ISC-Q index score

	Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
Ease of use					
1. It is easy to prepare my catheter for use each time I need it	☐	☐	☐	☐	☐
2. It is messy to prepare my catheter for use	☐	☐	☐	☐	☐
3. It is easy to insert my catheter	☐	☐	☐	☐	☐
4. I find inserting the catheter is uncomfortable sometimes	☐	☐	☐	☐	☐
5. The design of the catheter makes it easy to insert	☐	☐	☐	☐	☐
6. The catheter is fiddly to use	☐	☐	☐	☐	☐
7. The lubrication on the catheter makes it difficult to use	☐	☐	☐	☐	☐
8. I feel confident in my ability to use my catheter	☐	☐	☐	☐	☐
Convenience					
9. Storage of catheters at home is inconvenient	☐	☐	☐	☐	☐
10. Taking enough catheters for a weekend away is very inconvenient	☐	☐	☐	☐	☐
11. Taking enough catheters for a 2-week holiday is very inconvenient	☐	☐	☐	☐	☐
12. Disposal of my catheter is inconvenient when away from home	☐	☐	☐	☐	☐
Discreetness					
13. I find it easy to carry enough catheters around with me on a day-to-day basis	☐	☐	☐	☐	☐
14. I find it easy to dispose of my catheter when I am away from home	☐	☐	☐	☐	☐
15. My catheter is discreet	☐	☐	☐	☐	☐
16. I can use my catheter discreetly when I am away from home	☐	☐	☐	☐	☐
17. I can easily dispose of my catheter without it being obvious to people	☐	☐	☐	☐	☐
18. My catheter allows me to feel confident when away from home	☐	☐	☐	☐	☐
Psychological well-being					
19. I am self-conscious about my need to self-catherize	☐	☐	☐	☐	☐
20. I would feel embarrassed if people saw my catheter in its packet	☐	☐	☐	☐	☐
21. My need to use a catheter sometimes makes me feel embarrassed	☐	☐	☐	☐	☐
22. I worry that my catheter doesn't always empty my bladder fully	☐	☐	☐	☐	☐
23. My need to use catheters stops me from visiting friends and family as often as I would like	☐	☐	☐	☐	☐
24. I worry about the risk of long-term problems from using my catheter	☐	☐	☐	☐	☐

Appendix C: InCaSa questionnaire score

Items and dimensions of the Intermittent Catheterization Satisfaction Questionnaire (InCaSaQ. English translation of the original validated questionnaire written in French).

	Question	Not satisfied at all = 0	Slightly satisfied = 1	Satisfied = 2	Extremely satisfied = 3
Packaging	Concerning discretion and bulk of the package, are you?	0	1	2	3
	Concerning hygiene and robustness of the package, are you?	0	1	2	3
	Concerning the opening and possible fixation of the catheter, are you?	0	1	2	3
Lubrication	Concerning the means used for lubrication (spontaneous, gel, water. . .), are you?	0	1	2	3
Catheter itself	Concerning holding, pushing and insertion into the urinary meatus, are you?	0	1	2	3
	Concerning ease of progression and insertion comfort, are you?	0	1	2	3
	Concerning the ease with which you could void (length of the catheter and catheter accessories), are you?	0	1	2	3
After catheterization	Concerning the ease with which your catheter could be disposed of, are you?	0	1	2	3

Appendix D: Perception questions

Perception Questionnaire:

Handling	Very difficult	Difficult	Neither Difficult nor Easy	Easy	Very easy	Don't know
How was it to prepare the catheter						
How was it to insert the catheter?						
How was it to empty the bladder?						
How was it to withdraw/remove the catheter?						
How was it to clean the catheter						
How was it to store the catheter						
How was it to perform a hygienic catheterization?						
How was the overall experience (from preparation to storage/disposal) of the catheter						
Confidence and in control	**Strongly disagree**	**Slightly Disagree**	**Neither agree nor disagree**	**Slightly Agree**	**Strongly agree**	**Don't know**
It was possible to perform a hygienic catherization						
It was possible to perform the overall procedure (from preparation to storage/disposal) within reasonable timeframe						
I feel in control when inserting the catheter						
I feel confident when inserting the catheter						
I feel in control when withdrawing the catheter						
I feel confident when withdrawing the catheter						
Sensation	**Strongly disagree**	**Slightly Disagree**	**Neither agree nor disagree**	**Slightly Agree**	**Strongly agree**	**Not applicable (lack of sensation)**
It feels gentle to insert the catheter						
It feels gentle to withdraw the catheter						
I have felt resistance during withdrawal						
I have felt a blocking sensation during catheterization						
I have felt pinching/stinging during catheterization						
Satisfaction	**Strongly disagree**	**Slightly Disagree**	**Neither agree nor disagree**	**Slightly Agree**	**Strongly agree**	**Don't know**
I am satisfied with the catheter						
I would recommend the catheter to others						
I would like to continue using this catheter						
I am concerned about risk of infection						
Convenience	**Strongly disagree**	**Slightly Disagree**	**Neither agree nor disagree**	**Slightly Agree**	**Strongly agree**	**Don't know**
I found the overall procedure (from preparation to storage/disposal) convenient						

Appendix E: Catheter preference

- Preference (Which catheter do you prefer?
  - The singe use catheter
  - The reuse catheter
- Reason for preference (Why do you prefer this product over the other?)
  - Easier to handle
  - Easier to control
  - Better sensation
  - More satisfaction
  - More convenient
  - Other (text)

- Would you consider to swift to a re-usable catheter in the future? (Yes/No)

Following question to the subject, to be completed by PI or delegate:

- Reason for drop-out (in case of discontinuation prior to 28 test days)
  - Reason not stated by the subject
  - Inconvenient to use
  - I was concerned about getting an infection/UTI
  - It was difficult to handle
  - It was too time consuming to use
  - Lack of discretion
  - It was uncomfortable to use the catheter
  - Other (text)

Appendix F: Scales of measurements with Siemens dipstick

Scales of haematuria measured with a Siemens dipstick

1.	Negative	Negative	0 Eryt/µL	Negative	
2.	Trace	10 +/- (non-haemolysed)	10 Eryt/µL	Negative	
3.	Moderate	80 2+ (non-haemolysed)	80 Eryt/µL	Positive	
4.	Hemolyzed Trace	10 +/- (haemolysed)	10 Eryt/µL	Negative	
5.	Small/+	25 1+ (haemolysed)	25 Eryt/µL	Positive	
6.	Moderate/++	80 2+ (haemolysed)	80 Eryt/µL	Positive	
7.	Large/+++	200 3+ (haemolysed)	200 Eryt/µL	Positive	

Scales of leukocyturia measured with a Siemens dipstick

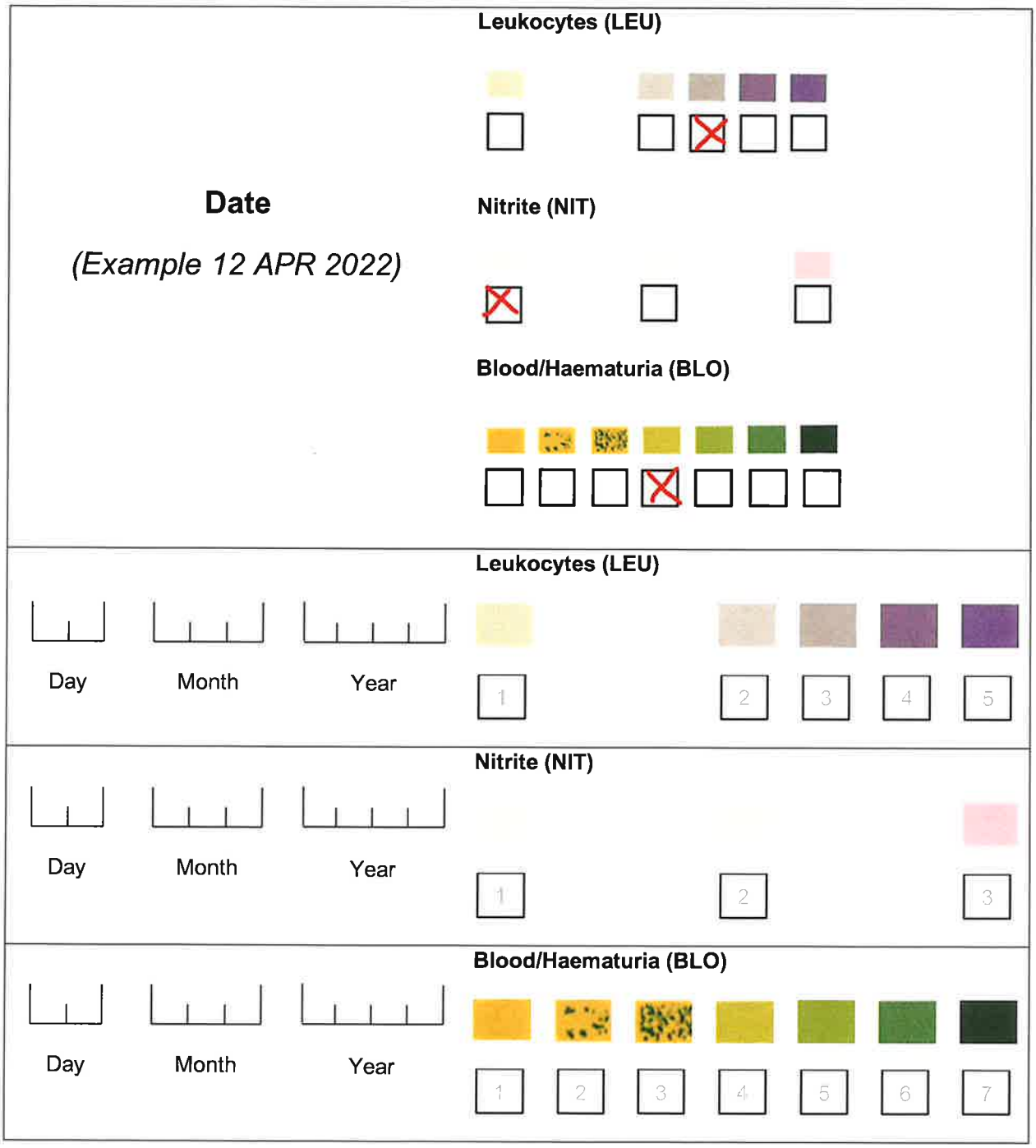
Negative 0 Leu/µL	15 Leu/µL1+	70 Leu/µL 2+	125 Leu/µL 3+	500 Leu/µL 4+
1.	**2.**	**3.**	**4.**	**5.**

Scales of nitrite measured with a Siemens dipstick

Negative	Positive (degree of uniform pink colour)
1.	**2.** **3.**

Appendix G: Weekly urine dipstick form (Siemens dipstick)

For Phone Call V2, V3 and V4



Appendix H: Endpoints and Assessments

	Endpoints and assessment	Assessed by	V1 (Baseline)	V2 (Phone Call)	V3 (Phone Call)	V4 (Phone Call)	V5 (Termination)
Primary endpoint	Health-related quality of life (HR-QoL) measured by intermittent self-catheterization questionnaire, (ISC-Q) index score at Baseline Visit (V1) and at the termination Visit (V5) Appendix A	**Subject**	X				X
Secondary endpoint	The secondary endpoint will be an evaluation of adverse events from time of signed informed consent and throughout the test period.	**Site**	X	X	X	X	X
Exploratory endpoints	Satisfaction of intermittent catherization measured by the InCaSa questionnaire score	**Subject**	X				X
	Perception questions (evaluated on a 6-point scale)	**Subject**	X				X
	Total catheter-associated bacterial count (CFU/mL)	**Coloplast Laboratory**	X				X
	Number of bacterial-positive catheter samples	**Coloplast Laboratory**	X				X
Assessments	Urine Dipstick for haematuria, leucocytes, and nitrite (Baseline Visit and Termination Visit the dipstick is performed at site). (Visit 2, 3 and 4 the dipstick will be performed by subject at home)	**Subject/Site**	X	X	X	X	X
	Preference (Appendix E)	**Subject**					X
	Reason for drop out if Termination Visit is performed prior to 28 test days	**Site**					X

	Endpoints and assessment	Assessed by	V1 (Baseline)	V2 (Phone Call)	V3 (Phone Call)	V4 (Phone Call)	V5 (Termination)
	Evaluation of catheterization since last visit: Have the subject used single use catheters since last Baseline Visit Did the subject follow all cleaning procedures stated in the IFU? Average number of daily catheterizations with CLINY the subject completed since last visit Average time spent on each catheterization from preparation to storage/disposal (in minutes)	**Subject/Site**		**X**	**X**	**X**	**X**
	Visual and microscopic evaluation of the CLINY catheters for defects (defects/no defects)	**Coloplast Laboratory**					**X**
	Electron microscopy scanning and confocal microscopic evaluation of the catheters surface (defects/no defects)	**Coloplast Laboratory**					**X**
	Changes in Concomitant medication	**Investigator**	**X**	**X**	**X**	**X**	**X**
	For female subjects of childbearing potential: urine pregnancy dipstick	**Subject/Site**	**X**				