Clinical Investigation Plan

CP326

Exploratory study of a new urine collection device for men

June 2020 – December 2020

1st of December 2020

NCT04672993

CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	DKTKSI	First approved version
2.0	DKCKI	Updated due to comments from Ethics Committee and minor internal changes Section 1.1 – Sponsor representatives: Contact information for Data manager and Clinical Manager have been updated. Section 6.2 – Recruitment and enrolment: Only potential subjects in the Coloplast Database, that have consented to be contacted regarding clinical investigations, will receive an invitation letter. Section 7.3 – Flow-charts: Some answers have been updated to be clearer.

SYNOPSIS OF THE CLINICAL INVESTIGATION

The aim of the study is to evaluate the subjects experience of the test product "Contend Protective Cover" - a urine collection device for males.

Objective

Primary objective:

- To investigate the comfort of using the test product.

Secondary objective:

- To evaluate handling and subject experience during wear in support of commercial claims.

Design of the investigation

An open-labelled, single arm study design was chosen for study CP326.

A single arm study over a duration of 1 week + up to 3 days extra

V0: Inclusion

V1: Test visit 1

V2: Test visit 2 and termination

Subjects may be interviewed up to two times either in-person or over the phone and these interviews will preferably be conducted at V2. Second interview can be conducted up to 6 months after V2.

Primary endpoint and secondary endpoint(s)

Primary endpoint:

- Frequency of success in support of "comfortable"

Secondary endpoints:

- Frequency of success in support of various commercial claims

Please see Table 2 for a detailed listing of all endpoints

Population/subjects

Twenty male subjects who are suffering from mild-to-moderate urinary incontinence, will be enrolled in this study.

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

Inclusion criteria:	Exclusion criteria
1. Have given written informed consent 2. Male	1. If experiencing incontinence less than once per week

3. Be at least 18 years of age and have full legal capacity 4. Suffering from urinary incontinence equivalent to using up to 6 pads or 2 diapers per day 5. Have had current incontinence issues for at least 3 months 6. Able to understand patient information and able to change the product himself 7. Up to 6 of the subjects can be user who are using an intermittent catheter due to retention, but who are also dribble incontinent in-between catheterizations, and hence need a product to handle the incontinence. 8. Able to fit the test product.	2. Bedridden, using wheelchair or using a walking aids daily.

Test products and comparator

The test product "Contend Protective Cover" is a leak tight pocket with an absorption material to be placed on the penis. The test product is a single use device which and should be changed when needed and minimum after 24h. 2 sizes will be tested: regular fit (Ø18) and large fit (Ø22).

The test product will be CE-marked prior to study start.

Investigation approval

The investigation will be approved by the Ethical committees in Denmark before initiation of the investigation.

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 16.2
AE	Adverse Event	See section 16.1
ASADE	Anticipated Serious Adverse Device Effect	See section 16.4.2
CFR	Code of Federal Regulation	
CIP	Clinical Investigation Plan	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection. See section 10.1
CM	Clinical Manager	
CRO	Clinical Research Organisation	See section 6.2
EC	Ethics Committee	
EDC	Electronic Data Capture	A software system designed for collecting clinical data in clinical trials. It consists of a data base for each clinical trial.
FDA	Food and Drug Administration	
IFU	Instruction For Use	
ITT	Intention to Treat	
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.
PP	Per Protocol	
SADE	Serious Adverse Device Effect	See section 16.4.1
SAE	Serious Adverse Event	See section 16.4
USADE	Unanticipated Serious Adverse Device Effect	See section 16.4.3

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1. List of personnel involved in the Investigation

1.1. Sponsor representatives

CLINICAL MANAGER	SENIOR BIOSTATISTICIAN
SCIENTIFIC MANAGER	**HEAD OF CLINICAL OPERATIONS**
DATA MANAGER	**MEDICAL ADVICER**

In case of emergency, please contact the Clinical Manager (CM) from the above list of sponsor representatives.

1.2. Investigators

The CM is responsible for maintaining an updated list of all Principal Investigators (PI's), investigation sites and institutions.

PRINCIPAL INVESTIGATOR

Visits will be conducted at subject's own home or at a clinic or at Coloplast A/S, if subjects prefer not to have visits at own home.

2. Introduction

The prevalence of urinary incontinence in adult men has been estimated to range between 11-34% in older men, and 3-5% in younger and middle-age men [1]. The products available for men with mild-to-moderate incontinent are typically adult pads or diapers, e.g. Tena for men. Pads and diapers are not always optimal, as they are seen as large/bulky to use and store, and there is a risk of leakage, if the pad/diaper displaces during use, and urinary leaks are not absorbed by the product.

Coloplast has developed a new product for men with mild-to-moderate urinary incontinence, which is placed directly on the penis, and where the absorber (pad) are placed in a water-tight pocket. The product is the size of the smallest incontinence pads on the market for men, and can fit into to pockets of most trousers.

3. Objective(s) and hypotheses of the clinical investigation

3.1. Objective (s)

The aim of the study is to evaluate the subjects experience of the test product "Contend Protective Cover" - a urine collection device for males.

The primary objective is:

- To investigate the comfort of using the test product.

Secondary objectives are:

- To evaluate handling and subject experience during wear in support of commercial claims.

3.2. Hypotheses

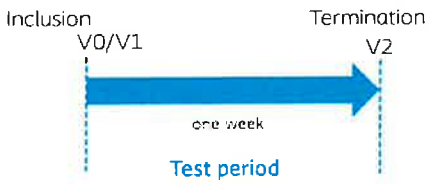
There is no formal hypotheses associated to this study.

The study will provide valuable insight into the use of the device in an everyday life setting.

4. Design of the clinical investigation

4.1. General

An open-labelled, single arm study design was chosen for study CP326 with a duration of 1 week + up to 3 days extra as illustrated below.



V0: Inclusion, V1: Test visit 1,

V2: Test visit 2 and termination

Subjects may be interviewed up to two times either in-person or over the phone and these interviews will preferably be conducted at V2. Second interview can be conducted up to 6 months after V2.

4.2. Endpoints and assessments

Primary and secondary endpoints are mentioned in this section on a high level. Endpoint details and flow-chart of measures are presented in Table 2.

4.2.1. Primary endpoint

Primary endpoint:

- Frequency of success in support of "comfortable"

4.2.2. Secondary endpoints

Secondary endpoints:

- Frequency of success in support of various commercial claims

Please see Table 2 for a detailed listing of all endpoints

4.2.3. Rationale for selection and measurement of endpoints

The endpoints selected for this study have been chosen to provide the information about the subjects' experience with the product. Information about comfort, handling and experience during wear are all important in understanding how the subjects use and evaluate the product.

4.2.4. Demography and potential compromising factors

Assessments:

- Age
- Level of incontinence (how often, how much)
- Usual product/management routine (using a product, what type, how many)
- Reason for incontinence (if known)
- Duration of incontinence (for how long has subject had the current issues)

4.3. Discussion of clinical investigation design

An open-labelled, single arm study design was chosen for this study with a duration of a test period of 1 week. The study cannot be blinded because only one test product is tested. The study period of one week is assessed as adequate for evaluation of the endpoints.

5. Investigational device and comparator(s)

5.1. Description of investigational device

The test product is a leak tight pocket containing an absorber to absorb urinary leaks, to be placed on the penis. The test product is a single use device which should be changed when needed and minimum after 24h. 2 sizes will be tested: regular fit (Ø18) and large fit (Ø22). The test product will be CE-marked prior to study start.

Figure 1: Investigational device

Subjects will be provided with a sufficient number of test devices

The turquoise line on the front side of device on the picture to the left, mark the pocket opening to be used when peeing while wearing the device. Back side of the device (facing the body) on the picture to the right, show the transparent flex collar, fixating the device on the penis.

5.1.1. Manufacture

Coloplast A/S, Holtedam 1-3, 3050 Humlebæk, Denmark, is the manufacturer of the CE marked test Product.

5.1.2. Identification, traceability and labelling of the device

The investigational test device will be identified as Contend Protective Cover.

Investigational device label Ref [3] can be found in IFU Ref [4]

5.2. Purpose of the device in the clinical investigation

The purpose of the device is to collect and contain urine from a male subject suffering from mild-to-moderate incontinence.

5.3. Intended population for the device

Males who are suffering from mild-to-moderate urinary incontinence once a week, are considered intended population for the device.

5.4. Handling and training

The handling of the test products is described in details in the Instruction for Use (IFU), which is included in all boxes with test products. Storage conditions are also stated in the IFU.

All Investigators / investigator representatives will receive training by sponsor / investigator in the handling and correct use of the test products. The Investigator/investigator representative will train the subjects in the correct use of the test products.

5.5. Ethical considerations, investigational device and clinical investigation risks and benefits

The clinical investigation is conducted in accordance with current law and applicable standards see section 14. The rights, safety and well-being of human subjects shall prevail over interest of science and society.

No risks are expected to the subjects other than the adverse events mentioned here, all of which are well known in connection with the use of absorbent product for urinary incontinence. Please see section 16.2. The risk assessment of the test products is carried out in accordance with the requirements of ISO 14971: 2007.

To mitigate and reduce risks, all subjects will be trained, according to the IFU, in the use of the product.

Expected benefits are a better fitted and more discreet product, tailored for men with mild-to-moderate urinary incontinence.

Disadvantages during the investigation could be the extra workload related to completion of questionnaires, visits at home or at a clinic or at Coloplast A/S, if subjects prefer not to have visits at own home.

5.6. Comparator product(s)

There is no comparator product in this investigation.

6. Subjects

Twenty male subjects who are suffering from mild-to-moderate urinary incontinence, will be enrolled in this study.

6.1. Inclusion and exclusion criteria

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

Inclusion criteria:	Justification:
1. Have given written informed consent 2. Male 3. Be at least 18 years of age and have full legal capacity 4. Suffering from urinary incontinence equivalent to using up to 6 pads or 2 diapers per day 5. Have had current incontinence issues for at least 3 months 6. Able to understand patient information and able to change the product himself 7. Up to 6 of the subjects can be users who are using an intermittent catheter due to retention, but who are also dribble incontinent in-between catheterizations, and hence need a product to handle the incontinence. 8. Able to fit the test product.	1. To meet the Helsinki Declaration 2. To meet the target population of this device 3. To meet the Helsinki Declaration 4. To meet the target population of this device 5. To be sure subjects meets target population of this device 6. To meet the Helsinki Declaration 7. To meet the target population of this device 8. To meet the target population of this device

Exclusion criteria:	Justification:
1. If experiencing incontinence less than once per week 2. Bedridden, using wheelchair or using a walking aids regularly	1. To meet the target population of this device 2. To meet the target population of this device

6.2. Recruitment and enrolment

Recruitment of potential subjects will begin once approval has been obtained from Ethics Committee.

Recruitment method	Coloplast Database	Advertisement	Patient records
Potential subjects	Recruitment will go through Coloplast own subject database (Intermittent Catheterization users) in Denmark. Potential subjects are identified by the following searching criteria in the Coloplast database: • Has consented to be contacted regarding clinical investigations • Using Intermittent Catheterization • Male • Be at least 18 years of age	Advertisement i.e. in local shops, sports facilities, local newspapers, social media and patient associations. The advertisement will state the contact info of investigator or delegated study personnel to contact. A CRO may help by receiving reply letters/mails and/or answering the phone from interested subjects.	Recruitment from hospitals, home care nurses and outpatient urology clinics will be via patient visit or screening of subject records kept at the participating sites. Only contact information regarding potential subjects who are assessed eligible will be passed on.
First contact	The identified potential subjects will as first contact be sent an Invitation and Reply Letter by mail or email.	Interested subject contact the investigator or delegated study personnel	The identified potential subjects will be contacted and informed about the investigation by the investigator or delegated study personnel (First contact will be by letter or e-mail, a follow-up contact can be via telephone, letter or e-mail).
	If a potential subject does not return the reply letter or answer the email, they may be contacted by phone, mail or email to make sure that they have received the approach.		
Second contact	If potential subjects return the Reply Letter/reply to the email, or have called the investigator as first contact and are interested, the Investigator or delegated site personnel will contact the subjects by phone and give a short introduction to the investigation and go over the inclusion and exclusion criteria. If the subjects do not meet the inclusion criteria or meet the exclusion criteria, this will be registered in the Subject Screening Log.		
Subject Information Form	If subjects are eligible and interested in participating, then written information about the investigation (subject information) will be sent to the subjects to ensure that they are given the opportunity to read about the investigation before a possible information visit, and so that they can prepare any possible questions they may have. Information visit V0 will be booked at this point and the subjects are instructed to contact the investigator or delegated study personnel if they, after having read the subject information, no longer are interested in participation in the study.		

First visit Information visit	If an eligible subject is interested in participating, information visit (V0) will be arranged in a room ensuring quiet surroundings. That could either be in the subject own home or at a clinic or at Coloplast if subject prefer not to have visits in own home. When arranging the visit, it will be ensured, that the subject has received the Subject Information prior to the visit. The subjects will receive both written and verbal information about the possibility of bringing a companion to the informational visit and to any possible subsequent visits. See section 15 for information to be given to the subjects, as well as the informed consent process.
Enrolment and inclusion visit (V0)	The subjects have the right to wait 24h before deciding on participation. If/when the subject decides to participate the subject will be asked to sign the relevant forms (see section 13). If a subject so desires, and it is certain that it is understood what the investigation entails and the relevant forms have been signed the subjects are considered enrolled in the investigation.

6.3. Subject withdrawal criteria

The subject can withdraw from the investigation at any time for whatever reason without any consequences for their future treatment outside the clinical investigation. 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:

- Non-compliance with the CIP impacting the scientific integrity of the investigation
- If subject's safety and wellbeing is compromised by further participation.

Withdrawn subjects will not be replaced by new subjects.

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, see section 16.

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 4.1.

6.5. Total expected duration of the clinical investigation

The dates below are approximate, and no subjects will be enrolled before required approval has been obtained.

- First subject enrolled (09/2020).
- Last subject enrolled (11/2020).
- Last subject completed (12/2020).
- Final report (12/2021).

7. Procedures

7.1. Clinical investigation-related procedures

Before initiation of the clinical investigation, sponsor must be provided with key 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 CRFs, procedure for reporting an adverse event or serious adverse event (how, when, to whom), and who to contact in case of emergency related to the investigational device.

See section 7.3 Flow-charts for a more detailed overview of the clinical investigation-related procedures at visits, phone visits and at product/baseplate change.

7.1.1. Visits

Visit 0 (Inclusion visit)
If a potential subject is interested in participating after the first contact, a visit (visit 0) will be arranged at subject's home or at a clinic or at Coloplast, if subjects prefer not to have visits in own home, in a room reserved to ensure privacy and quiet surroundings. When arranging the visit, it will be ensured, that the subject has received the Subject Information Form prior to the visit. The subjects will receive both written and verbal information to ensure that the subject understands what was read and explained and can freely agree to participate in the investigation. The subject will, beforehand, also be informed about the possibility of bringing a companion to Visit 0 and to any possible subsequent visits. During the visit the principal Investigator, or delegate, will provide oral information about the investigation based on the Subject Information Form. The subject has the right to wait before deciding on participation.

If/when subjects decide to participate, they will be asked to sign the Informed Consent Signature Form. If a subject so desires, and it is certain that it is understood what the investigation entails, and the relevant form has been signed, the subjects are considered enrolled in the investigation. Enrolled subjects that are deemed eligible per the inclusion/exclusion criteria are allocated a subject number. Visit 0 and visit 1 can be combined.

Visits 1 (V1)
During visit 1, part 1 of the questionnaire Table 1 (demographic questions) will be completed by the Principal Investigator, or delegate. The subject will be trained in the use of the test product per IFU. The subjects are instructed to continue their everyday life and change test product whenever they feel the need to.

Visits 2 (V2)
During visit 2, the Principal Investigator, or delegate will ensure part 2 of the questionnaire Table 2 will be completed by subjects. Potential (S)AE's will be captured by the Principal Investigator, or delegate. Hereafter termination If appropriate, subjects may be interviewed regarding use of the test product by a Coloplast representative at V2, otherwise an alternative time for interview may be scheduled.

7.2. Activities performed by sponsor representatives

Sponsor (Clinical Manager or a representative hereof) is responsible for:

1. Training of investigator and study personnel in the informed consent procedure, study procedures,
    a. how to use the products, complete the CRF, how to report possible safety issues and in ISO 14155.
    b. All training will be documented by site
2. Support during the recruitment process and conduct of the investigation
3. Monitoring

7.3. Flow-charts

Table 1: chart showing the connection between visits and assessments

Assessment General	Type of assessment	Assessed by	V0/V1	V2
Oral information		Investigator	X	
Written informed consent	Informed Consent Form	Subject	X	
Consent to interview	Informed Consent Form - Interview	Subject	X	
Check of inclusion and exclusion criteria	CRF	Investigator	X	
Subject number allocated		Investigator	X	
Assessment	**Type of assessment**	**Assessed by**	**V0/V1**	**V2**
Demographics • Age • Level of incontinence (how often, how much) • Usual product/management routine (using a product, what type, how many) • Reason for incontinence (if known) Duration of incontinence (for how long have subject had current issues)	Part 1 questionnaire	Investigator	X	
Endpoint assessment: • **Comfortability** • **Handling** • **Subject experience of use**	Part 2 questionnaire (Table 2)	Subject		**X**

Registration of AEs/SAEs	AE/SAE form	Investigator		X
Termination	Termination form	Investigator		X

Table 2 chart showing the connection between visits and endpoints.

Assessment	Type of assessment	Assessed by	V0/V1	V2	Derived from
Endpoint	**Questions UK**				**Answers UK**
Frequency of success in support of "comfortable"	How comfortable was the product to wear?	Subject		X	Very uncomfortable – uncomfortable – neither uncomfortable nor comfortable – comfortable – very comfortable
Frequency of success in support of "easy to apply"	How was the product to apply?	Subject		X	Very difficult – difficult – neither difficult nor easy – easy – very easy
Frequency of success in support of "easy to remove".	How was the product to remove?	Subject		X	Very difficult – difficult – neither difficult nor easy – easy – very easy
Frequency of success in support of "easy to urinate during wear".	How was it to urinate normally while wearing the product?	Subject		X	Very difficult – difficult – neither difficult nor easy – easy – very easy

Frequency of success in support of "no product awareness during wear"	While wearing the product, how aware were you of wearing it?	Subject		X	Noticed all the time – noticed some of the time – Don't know – didn't noticed much – didn't noticed at all
Frequency of success in support of "easy to open/close functionality"	How was it to use the open/close functionality at the front of the product?	Subject		X	Very difficult – difficult – neither difficult nor easy – easy – very easy
Frequency of success in support of "feeling secure"	How was your feeling of security while wearing the product?	Subject		X	Very poor – poor – neither poor nor good – good – very good
Frequency of success in support of "discreetness during wear	How discreet did you find the product during wear?	Subject		X	Very indiscreet – indiscreet –Don't know– discreet – very discreet
Frequency of success in support of "discreetness during urinating using the opening"	How discreet did you find the product when you needed to urinate by using the opening at the front?	Subject		X	Very indiscreet – indiscreet – Don't know – discreet – very discreet
Frequency of success in support of "discreetness in the level of urine smell"	How discreet did you find the smell of urine from product?	Subject		X	Very indiscreet – indiscreet – Don't know – discreet – very discreet

Frequency of success in support of "discreetness in the level of noise"	How discreet did you find the noise from product, while you were wearing it?	Subject		X	Very indiscreet – indiscreet – Don't know – discreet – very discreet
Frequency of success in support of "living the life you want"	To what extend do you agree in the following statement: The product supports me in living the life I want	Subject		X	Strongly disagree – disagree – Don't know – agree – strongly agree
Frequency of success in support of "the feel of confident management"	How confident were you that you could manage your incontinence while wearing the product?	Subject		X	Very insecure – insecure – Don't know – confident – very confident
Frequency of success in support of "a dry feeling"	Did the product give you a dry feeling?	Subject		X	Not at all – no –Don't know – yes – yes very much
Frequency of success in support of "a good fit – flex collar"	Did the flex collar provide a good fit?	Subject		X	Not at all – no – To some degree – yes – yes very much
Frequency of success in support of "a good fit – whole product"	Did the whole product provide a good fit?	Subject		X	Not at all – no – To some degree – yes – yes very much

Frequency of success in support of "stays in place"	Did the product stay in place during use?	Subject		X	Not at all – no – Don't know – yes – yes very much
Frequency of answers pertaining to yes in support of "future use"	If, possible, would you want to use the product in the future?	Subject		X	Yes - No
Frequency of answers pertaining to yes in support of "reliability for in-home use"	Do you rely on the product being functional for use a home?	Subject		X	Yes - No
Frequency of answers pertaining to yes in support of "reliability for use away from home"	Do you rely on the product being functional for using away from home? By this we mean e.g. at work, during sports, being social or when traveling.	Subject		X	Yes - No
Frequency of answers pertaining to yes in support of "future recommendation"	Would you recommend the product to others?	Subject		X	Yes - No
Frequency of answers pertaining to yes in support of "preference"	Do you prefer this product over your normal product / normal management routine?	Subject		X	Yes - No

Additional assessments					
	What size product did you use	Subject		X	Large – Regular - both
	If both – which size did you prefer	Subject		X	Large - Regular
	How many products did you typically use per day?	Subject		X	• 1 • 2 to 3 • 4 to 5 • 6 or more
	In average, for how long did you typically use one product? (categories)	Subject		X	• 1-2 hours • 3-4 hours • 5-6 hours • 7-12 hours • More than 12 hours
	Where did you use the products? (categories, more answers are allowed)	Subject		X	• At home • At work • At social event(s) • While doing sports • During travel/trip At night
	Did you experience leakage? (Y/N)	Subject		X	Yes - No
	If yes – when? (categories, more answers are allowed)	Subject		X	• While sitting • While standing • While moving about • While laying down Other, please describe____

	If yes – how often? (categories, more answers are allowed)	Subject		X	• Several times a day • Once a day • 5-6 times during the week • 2-4 times during the week 1 during the week

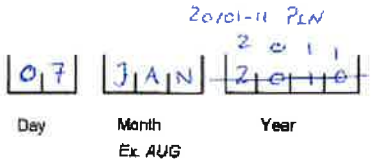
7.4. Case Report Forms

All assessments and observations throughout the investigation must be carefully recorded in an electronic CRF (eCRF). Details about data capture can be found in section 10.1

Forms that need subject signature will be present in paper format (pCRF).

Any correction in the pCRF must be clearly signed and dated by authorised site personnel. The entry corrected must be crossed out so that the entry is still legible.

Example 1:



Example 2:

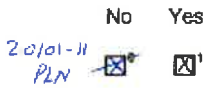


Figure 2 Two examples of how to make corrections in the pCRF

7.5. Concomitant treatment

Concomitant treatment, including relevant medication, will be registered in the CRF.

7.6. Supplementary materials and equipment (if applicable)

The Sponsor will provide the Principal Investigator, or delegate with supplementary materials for this investigation. Supplementary materials would be:

- Computer or Iphone with access to eCRFs
- Nurse kits including disposal bags, gloves, gauze, disinfection gel etc.

8. Monitoring and source data verification

All data collected will be directly entered into the eCRF and the EDC system will via edit checks ensure that all fields are completed in the eCRF.

The Informed Consent Forms and (S)AE/ADE will be 100% monitored for timely completeness. eCRF's will be remotely monitored with regards to completeness.

Only the investigator, delegated site personnel and the sponsor representatives will have access to all the eCRFs. The subject will have access to his/her own CRF.

8.1. 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 investigation 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 too little variance)

- Special attention will be given in case of frequent data anomalies or errors, protocol violations or excessive drop outs.
- 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 indicative of systemic and/or significant errors in data collection and reporting at the site
- Verify source data remotely, provided that both source data and CRFs can be accessed remotely
- Conduct aggregate statistical analyses of study data to identify subject data that are outliers relative to others and to evaluate individual subject 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

8.2. Other methods for data quality assurance

The sponsor, sponsor's representative and/or investigational sites may be inspected by competent authorities or their representatives and likewise may be audited per Coloplast's internal quality audit plan and procedures. The investigator allows access to source data, medical records and other relevant documents for this study both for monitoring, audit and/or inspections from the Ethics Committee and competent authorities.

9. Statistical considerations

9.1. Statistical design, method and analytical procedures

Endpoints and assessments

All baseline assessments, endpoints and other measurements will be reported by descriptive statistics and/or listed.

Analysis populations

Intention to Treat (ITT), Safety and Per Protocol (PP) populations will be defined at a formal data review meeting just before database lock. As a minimum, the clinical manager and the statistician will be involved in the classification of subjects.

The Safety population (basis for the AE summary) will constitute subjects with valid informed consent.

The ITT population (Full analysis set) will constitute all subjects, with valid informed consent, who have been exposed to at least one product and furthermore, with information recorded on at least one endpoint (non-missing).

No formal PP population is planned. However, if additional explorative analyses are deemed necessary, a PP population will be established, based on a subset of the ITT population.

Individual endpoints/data points may be excluded from analysis, even though the corresponding subject belongs to the ITT population. This situation could arise due to protocol violations, where, at one visit, the primary endpoint could be affected, but same effect did not occur at the following visit.

All analysis will be based upon the ITT population and AEs will be summarized based on the safety population.

Any exclusion of subjects or data points from any of the populations must be documented.

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.

A significance level of alpha equal to 0.05 (two-sided) is applied.

All endpoints will be analyzed by an exact test in the binomial distribution (proportion is equal to 50%), where the frequency of success or will estimated with 95% confidence limits.

The two highest or best categories in questions obtained from a 5-point ordinal scale is defined as a success. Likewise, the answer yes, is defined a success, obtained from questions with a yes/no categorical option.

In favor of a claim, the lower 95% confidence limit must be above 50%.

Other summaries and analyses can be made, if relevant.

All statistical analyses and summaries are made with SAS version 9.4 (SAS Institute Inc., Cary, NC)

9.2. Sample size

Due to the conceptual nature of this trial no formal sample size calculation has been performed. It is assumed that 20 subjects will be adequate for evaluating the comfortability of the test product.

We strive to include subjects representing most possible age groups in the study.

Due to the exploratory nature of the study, drop-out subjects will not be replaced.

9.3. Level of significance and power

If a statistical analysis is performed a significance level of 5% will be applied. As this is an exploratory study no power has been applied.

9.4. Pass/fail criteria

The study is conducted as a proof of concept study.

Pass criteria is defined as: In favor of a claim, the lower 95% confidence limit must be above 50%.

9.5. Interim analysis

There is no planned interim analysis in this investigation..

9.6. Statistical reason for termination of investigation

There will be no interim analysis and therefore no reason to terminate the investigation based on statistical considerations.

9.7. Deviation(s) from statistical design, method or analytical procedures

Any deviations from the statistical plan will be documented in the clinical investigation report.

10. Data management

10.1. Data Collection in the clinical investigation

Data management and the final statistical analyses of all measurements described in this protocol are carried out by the Medical Affairs, 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 defin[illegible]

The EDC system used is[illegible] 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 (medical records) 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.

Adverse events should be registered following the timelines described in the Adverse Event section.

When subject and investigator is required to complete different sections in the CRF, it will be specified which sections the subject will fill in and which sections the investigator will fill in. Please see the flow chart section 7.3 for details.

Additional data from other apps or external companies will be batch loaded into the EDC system.

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.

10.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The principal investigator or dele-gate must be trained in the system prior to getting access. The training is web-based and must be complet-ed before access to the investigation is granted. Training will be documented in the data management sys-tem. 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 SOP's.

10.3. Data retention

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

All investigation site documents will be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

11. Amendments to the CIP

Any significant changes to the CIP are:

- Agreed between sponsor and PI
- Justified in a statement included in the amended section and the version number and date of amendment must be documented
- Registered in the Change Log
- Notified to or approved by the EC before implementation
- Notified to or approved by the regulatory authorities before implementation

Example of significant change: Changes of inclusion criteria, end points or assessment methods.

12. Deviations from Clinical Investigation Plan

The Investigator is not allowed to deviate from the CIP unless under emergency circumstances and to protect the rights, safety and well-being of the subject(s). Deviations must be reported to sponsor and deviations affecting the scientific aspect of the investigation or the safety of the subject are reported to the EC by sponsor if required.

In case of continued or repeated deviations affecting the scientific aspect of the investigation or the subjects' rights, safety and well-being sponsor will disqualify the Investigator from further participation in the investigation.

13. 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 per this CIP.

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

- Date of recept
- Identification of each investigational device (batch no./serial no./unique code) and number received
- Number of devices used
- Subject identification
- Identification of each investigational device (batch no./serial no./unique code) and number returned
- Date of returned investigational device

14. Statement of compliance

The clinical investigation is conducted in accordance to:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th 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 2017/45.
- GDPR: Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).
- ISO 14155:2011 "Clinical Investigation of medical devices for human subjects – Good clinical practices".
- Any applicable regional or national regulations will be specified in the country specific CIP.

14.1. Ethics committee and regulatory authorities

The investigational device will be CE-marked prior to study start and used per IFU. The CIP 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 has been obtained. Any amendment to the protocol will be submitted to the same EC(s).

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

14.2. Data protection

All personal data are kept as long as required by applicable laws and regulations. The EU Medical Device Regulation obliges Coloplast to retain data for a period of at least ten years after the end of testing, or in the event that the product is subsequently marketed, for at least ten years after the last product has been placed on the market. All personal information will be deleted at the end of the mandator retention period. Data will be stored by the vendor of the data management system Medidata Solutions in the US.

Each subject is entitled to get access to all the data and to have rectified any inaccurate data Coloplast is processing about the subject. All data are collected based on the consent each subject has given when being eligible and enrolled in the investigation. The subject is entitled to withdraw the consent at any time, and Coloplast will then cease to use such personal information for further innovation and improvement of products. The already data collected and handled in the investigation will not be retired.

The subject will be requested to check **www.coloplast.com/global/privacy-notice** for further information about the Coloplast's Global Privacy Notice. This will be described in the Subject Information Form/informed Consent Form.

All information collected during this investigation is kept strictly confidential. Subjects are identified by an investigation number and the investigation monitor has limited access to subjects' notes/documentation for source data verification. Any information which could identify a subject remains with the investigator where it is archived with investigation documents. Subjects remain anonym for data analysis. If payment to a subject's bank account is needed (*e.g.* transportation reimbursement) it may be necessary to collect subjects' social security number, which will then be confidentially handled.

Should the investigation require future review, relevant regulatory authorities and ethics committees will be allowed access to all relevant information for audit and inspection purposes.

Information collected at interviews will be archived confidentially and safe, as all other collected data in this investigation. User Insight works with the usability of the developing Coloplast products, and all collected data from interviews will in general be used in the product development at Coloplast A/S. The collected data will at that time be taken out of the specific relevant interview and context, and the subject, who has participated with this kind of data, is not able to identify.

14.3. Indemnity

14.4. Financial conditions

Coloplast A/S has taken the initiative to this study and Coloplast A/S will compensate all investigators involved in the clinical investigation for their time and resources spent on the investigation. The expenses include the salary to the Principal Investigator and study nurses, the cost of test products, shipments, transportation and gift certificates. The Principal Investigator and study nurses have no financial interest in the investigation. The total budget for the investigation is [redacted] covering 20 participants, each participating in 2 test visits. The expenses are paid on an ongoing basis All financial agreements with the investigation sites involved in the clinical investigation will be specified in a sponsor investigator Agreement.

Subjects will be paid for their participation in the study and receives a gift voucher equivalent in value to [redacted] visit 1 and 2, in [redacted] the subject completes the investigation. If interviews will be conducted, subjects will be paid for their participation in the interview and receives a gift voucher equivalent in value to [redacted] interview, in [redacted] if the subject completes two interviews.

15. 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 and 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/hers 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 Coloplast CM is responsible for writing the information and providing it 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.

This procedure also applies to informed consent obtained from a subject's legal representative. The procedure cannot waive the subjects' legal rights.

16. Adverse events, adverse device effects and device deficiencies

16.1. Adverse events

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other parties, whether or not related to the medical device(s), or the procedures involved. This could include events such as headache or dizziness.

16.2. 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 related or possibly related 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, e.g. mounting of the medical device, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

The anticipated adverse device effects are well known adverse events from the use of the investigational device.

Table 3 Anticipated adverse device effects and their likely incidence rates

ANTICIPATED ADE	INCIDENCE RATE
Skin irritation, intact skin (area covered by the product) [1]	3-25%
Allergic skin irritation [2]	< 1%

16.3. Device deficiency

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

Example: Contend Protective Cover is leaking due to insufficient welding

16.4. 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 fetal distress, fetal death or a congenital abnormality or birth defect

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.

16.4.1. 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.

16.4.2. Anticipated serious adverse device effect (ASADE)

Anticipated serious adverse device effect is any event that by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

16.4.3. 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.

16.5. Medical care of subjects

Principal investigator shall ensure that adequate medical care is provided to a subject experiencing an adverse event during and after participation in the clinical investigation. All serious adverse events will be followed until a resolution is addressed.

The current status of all ongoing adverse events is documented during site close-out.

16.6. Reporting and timelines

16.6.1. Investigators 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 must be reported to sponsor within 10 days of becoming aware of the event.

When reporting the SAE, the relationship to the investigational device 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.
- **Possibly 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 were relatedness cannot be assessed or no information has been obtained should also be classified as possible.

- **Probably 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.

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

Please report to:

16.6.2. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported to national regulatory authorities and ethics committees, as applicable, 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 two calendar days after awareness by sponsor report the event to national regulatory authorities and ethics committees, as applicable.

17. 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 EC(s) as applicable. 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 investigation site. The sponsor or investigator will inform the regulatory authority as the EC as applicable, about the termination of the site.

If suspension or termination of the clinical investigation occurs, the investigator(s) will promptly inform the enrolled subjects. Sponsor will provide resources to fulfil the obligations from the CIP for follow-up of the subjects as necessary.

18. Clinical investigation report

At completion of the 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 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 investigator(s) should be obtained.

The clinical investigation report must be submitted to EC and regulatory authorities, if the investigation has been subject to approval from regulatory authorities.

19. Publication policy

Coloplast, 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, e.g. www.ClinicalTrial.gov, before recruitment of the first subject. The results of the investigation, positive as well as inconclusive and negative will be published in the same public accessible database. The subjects' identity will remain confidential. Publication of results in the database will be conducted per the law of personal data protection and will be initiated as soon as scientifically acceptable, however, within one year after the last subject has completed the investigation. Data from the investigation is considered confidential until it is published per the conditions of this CIP and the 'Clinical Publication Policy'. Sponsor may publish anonymous single subject case stories at any time during and after the investigation. The identification of the subjects must not be possible. Sponsor reserves the right to use the data (published and unpublished) for reimbursement or regulatory purposes.

20. Bibliography

[1] Abrams,P, Cardozo, L, Wagg, A, Wein, A. (Eds) Incontinence 6th Edition (2017). ICI-ICS. International Continence Society, Bristol UK, ISBN: 978-0956960733. PP 2385.

[2]

[3] Clinical Investigation Device Label CP326, Doc. No: VV-0287510

[4] Instruction for Use CP326, Doc No: VV-0287489