Clinical Investigation Plan

CP321

Investigation of a supporting ostomy product intended for leakage detection

April 2021- June 2022

CHANGE LOG

VER-SION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	First approved version
2.0	[redacted]	Front page+p.15: Timeline changes from start February to start April P 17 added: In the Coloplast database potential subjects are identified by the following search criteria: subjects who have consented to be contacted for future clinical investigations, has ileostomy or colostomy and be at least 18 years of age.

SYNOPSIS OF THE CLINICAL INVESTIGATION

The aim of the study is to investigate the performance of a new supporting ostomy product. The intended purpose of the test product is to detect leakage beneath the ostomy baseplate and inform the user about this through a notification given on a smartphone handed out to subjects.

Title: Investigation of a supporting ostomy product intended for leakage detection

Test products and comparator

The test product consists of the following:

- Adhesive Sensor Layer
- A Transmitter which is connected to the Sensor Layer
- An app (Installed on a smartphone handed out to the subjects) The app is communicating sensor status to the user
- Charger to the transmitter
- Cable to the charger

No comparator is used is this study

Intended purpose: The sensor layer system is intended to be used together with an ostomy baseplate and bag, to detect and notify user of the occurrence of output leakage under an ostomy baseplate

Objective(s)

The primary objective is:

- The primary objective is to evaluate the system performance of the test product

Secondary objectives are:

- To evaluate reliability of notifications
- To evaluate user experience to support commercial claims
- To explore quality of life

Design of the investigation

Single arm design. Open-labelled

Study duration: 21 days + 3 days.

Study visits will be conducted remotely via video calls/phone calls if technical possible. If considered necessary by the study nurse, the visits can take place either in subjects own home or at a test facility at Coloplast.

V0: Inclusion

V1: Baseline demographics & evaluation (questionnaire) & Introduction to test product, start test period

V2: Termination

Vx: Follow up visits if needed

Primary endpoint and secondary endpoint(s)

Primary endpoint:

- The primary endpoint is to evaluate system performance focusing on accuracy of data classification into true positive and true negative

Secondary endpoints:

- Frequency of leakage onto clothes before and after use of test product
- Experience of leakage onto clothes compared to only using usual product
- Reliability of notifications
- Ability to move with test product
- Subjects worry of leakage before and after use of test product
- Confidence to avoid full leakage with test product compared to only using usual product
- Confidence in daily life compared to only using usual product
- Feeling of control with test product compared to only using usual product
- Control of leakage progression with test product compared to only using usual product
- Feeling of security with test product compared to only using usual product
- Evaluation of confidence to increase social activities with test product compared to only using usual product
- Evaluation of sleep with test product compared to only using usual product
- Confidence at night with test product compared to only using usual product
- Evaluation of users' preference
- Reason for preference
- Evaluation of users' peace of mind with test product
- To evaluate users' assessment of QoL with test product compared to usual product
- Adhesive residue to transmitter
- Adhesive residue to skin

Population/subjects

We will include n=25 subjects as a minimum of 25 subjects are needed to evaluate sensor performance and to have a potential support of relevant core claims.
N=15 subjects will get the test product app on an Android phone and n=10 users will get the test product app on an Iphone.

We strive to include an equally number of subjects in the categories 1pc, 2pc.

Subjects may use any Coloplast baseplate (Assura, SenSura, SenSura Mio) flat, convex and concave
Up to 5 subjects may use a mouldable ring (see exclusion criteria)

Inclusion criteria:

1. Have given written informed consent
2. Be at least 18 years of age and have full legal capacity
3. Have had a stoma for more than three months
4. Have intact skin on the area used in the evaluation meaning no broken skin and only minor discoloration of the skin (assessed by investigator)
5. Be able to use one of the five sensor layer sizes (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm)
6. Ileo- or colostomists with liquid output (Bristol scale type 6-7).
7. Currently using a Coloplast product (1pc/2pc Flat/Convex/Concave) from e.g Assura/SenSura/SenSura Mio
8. Have self-reported problems with leakage* (three times within 14 days)
9. Have worry of leakage 'to some, high or very high degree'
10. Is familiar with the use of a smartphone

*Leakage: Leakage is defined as output from the stoma on the backside of the baseplate (underneath the baseplate)

Subjects who uses a mouldable ring may be included, if able to fit one of the five test products while wearing the ring. The sensor layer should be applied to the peristomal skin, not covering the ring.

Exclusion criteria

1. Currently receiving or have within the past 2 month received radio- and/or chemotherapy
2. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment.
3. Are pregnant or breastfeeding
4. Participating in other interventional clinical investigations or have previously participated in this investigation. Exception: Participation in other Coloplast sponsored clinical investigations is accepted under the circumstances that the subject has paused the activities in the investigation and are otherwise complying with the inclusion and exclusion criteria of this protocol.
5. Known sensitivity towards test product
6. Known sensitivity towards acrylate
7. Is using/have a pacemaker
8. Is using ostomy paste or ostomy powder

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 18.2
AE	Adverse Event	See section 18.1
ASADE	Anticipated Serious Adverse Device Effect	See section 18.4
CIP	Clinical Investigation Plan	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection
CM	Clinical Manager	
DQF	Data Query Forms	A DQF is a query specifically used in clinical research. The DQF is the primary data query tool from the sponsor to clarify discrepancies and ask the investigator for clarification. The DQF is part of the data validation process in a clinical investigation.
DD	Device deficiency	
EC	Ethics Committee	
IB	Investigator's Brochure	Compilation of the current clinical and non-clinical information on the investigational medical device(s,) relevant to the clinical investigation.
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 18.4.1
SAE	Serious Adverse Event	See section 18.4
USADE	Unanticipated Serious Adverse Device Effect	See section18.4.3

> TABLE OF CONTENTS

1. List of personnel involved in the Investigation

1.1. Sponsor representatives

CLINICAL MANAGER	SENIOR BIOSTATISTICIAN
[redacted]	[redacted]
SENIOR SCIENTIFIC MANAGER	**HEAD OF CLINICAL OPERATIONS**
[redacted]	[redacted]
SENIOR DATA MANAGER	
[redacted]	

In case of emergency, please contact the CM from the above list of sponsor representatives.

1.2. Investigators

The CM is responsible for maintaining an updated list of all PIs, investigation sites and institutions.

PRINCIPAL INVESTIGATOR
[redacted]

2. Rational/justification for conducting the clinical investigation

People with intestinal stomas (especially an ileostomy) can have, despite development of better ostomy products, problems with leakage which influence their quality of life negatively [1,2].

To overcome this, Coloplast has developed a new supporting ostomy product, which has an adhesive sensor layer that should be place underneath the baseplate. The sensor layer consists of an electronic sensor system, that continuously detects moisture and output leakage underneath the baseplate. A transmitter connected to the sensor layer continuously evaluate the incoming information and sends a status to a

smartphone software application, which based on a predefined flow decides which information to deliver to the user about the baseplate status.

The purpose of this study is to investigate the sensor performance of this new supporting product with a test product app that is either used from an iPhone or an Android (Samsung) phone. The target population in this investigation is subjects with either an ileostomy or colostomy, who have liquid output and self-reported problems with leakage. Based on the results obtained in this study, new and better ostomy devices that can help detect leakage can be developed.

Two previous exploratory studies have been conducted (CP278 and CP308) [3+4]. In the first study (CP278) it was shown that the sensor technology worked, [redacted] The [redacted]

Based on the results obtained in the present investigation, new and better ostomy devices can be developed that help improving the users confidence and HRQoL.

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

3.1. Objective (s)

The primary objective is:

- The primary objective is to evaluate the system performance of the test product

Secondary objectives are:

- To evaluate reliability of notifications
- To evaluate user experience to support commercial claims
- To explore quality of life

The study is conducted as an exploratory study with no formal hypotheses.

4. Investigational device and comparator(s)

Subjects will test the test product for 21+3 days. The test product is used in combination with the ostomy baseplates usually used by the subject. Subjects will be supplied with a sufficient number of test products (sensor layers) to support their normal change routine.

4.1. Description of investigational device

The investigational device consists of the following:

- Adhesive patch - sensor layer
- Transmitter
- Sensor app (Installed on the smartphone handed out to the subjects). The app is communicating sensor status to the subject
- Charger to the transmitter

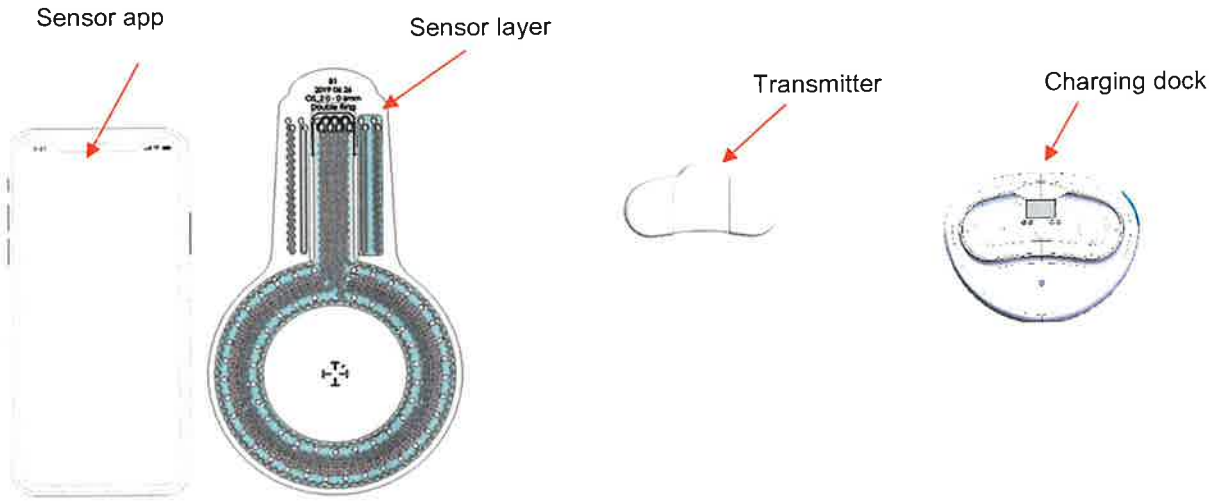
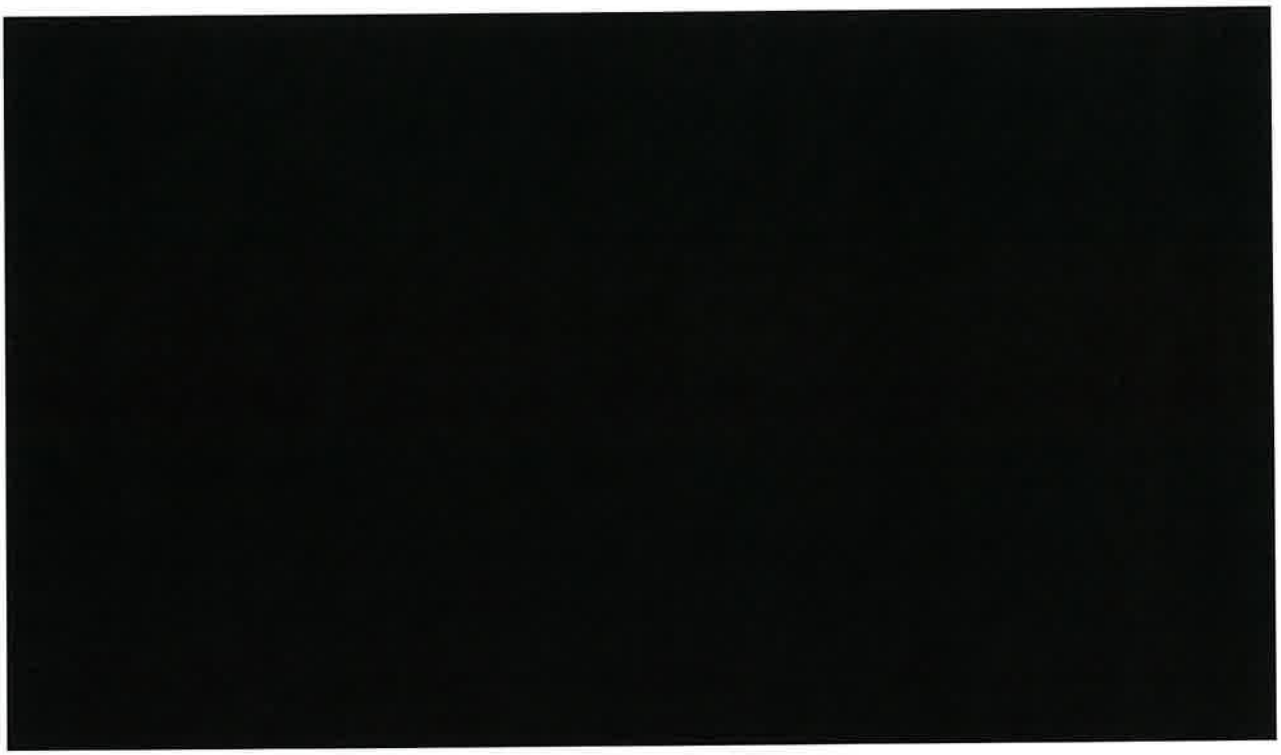


Figure 1: Investigational device

Subjects will be provided the device including a spare transmitter and sufficient number of adhesive sensor layers



The following sensor layer sizes will be available in the study: ø40, ø50, ø60, ø70 and ø80, referring to the inside diameter of the sensor layer. The study nurse and subject will together find the right size of sensor layer that best fit the subject.

4.1.1. Manufacturing

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

4.2. Identification and traceability of the device

The investigational test device will be identified as CP321/1

Investigational device label Ref [9] can be found in IB [11]

4.3. Intended purpose of the device in the clinical investigation

Intended purpose of device:

The sensor layer system is intended to be used together with an ostomy baseplate and bag, to detect and notify user of the occurrence of output leakage under an ostomy baseplate.

Intended medical indication(s):

The product is indicated for users with an ostomy, mainly Ileostomy and colostomy with liquid output.

The product is to be used on intact skin.

Intended mode of action:

The sensor layer is applied under an ostomy baseplate that is then attached to an intact peristomal skin around the stoma. The sensor layer detects occurrence of output leakage under the ostomy baseplate and the user is notified of the leakage via a smartphone software application.

Application:

In the Instruction for Use (IFU), application, few warnings, cautions and pre-caution of how to use test product are given. See IFU in Investigators Brochure (IB) [11]

4.4. Intended population for the device

Subjects with ileostomy or colostomy with liquid output are the intended population for this device.

4.5. Handling of the investigational device

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

4.6. Total number of devices intended for the clinical investigation

Subjects will be delivered one test product per day and 6 extras. Subjects will be delivered a starter box and retail boxes with sensor layers (10 in a box)

Each subject will be supplied with test products and study supplies as described below:

- 1 phone (iPhone or Android) with a specially designed application installed
- 1 charger
- 1 charging cable
- 1 charging adapter
- Two transmitters
- Test products to support a daily change pattern + 6 extra
- One iPhone for the Clinical Trial App

4.7. Description of the comparator product(s)

No comparator is used is this study.

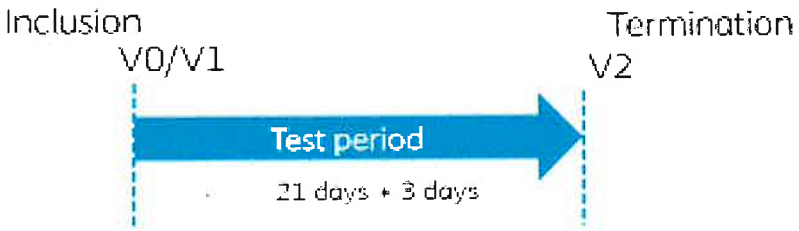
5. Design of the clinical investigation

5.1. General

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

Study duration: 21 days + 3 days.

Study visits will be conducted remotely via video calls/phone calls if technical possible. If considered necessary by the study nurse, the visits can take place either in subjects own home or at a test facility at Coloplast.



V0: Inclusion

V1: Baseline demographics & evaluation (questionnaire) & Introduction to test product, start test period.

V2: Termination

Vx: Follow up visits if needed

21 days are considered sufficient to meet endpoints of performance of the sensor layer, user experience with test product and to observe trends in changes of quality of life. The visit window of 3 days is chosen for flexibility purposes.

5.2. Primary endpoint

- The primary endpoint is to evaluate system performance focusing on accuracy of data classification into true positive and true negative

5.3. Secondary endpoints

Secondary endpoints:

- Frequency of leakage onto clothes before and after use of test product
- Experience of leakage onto clothes compared to only using usual product
- Reliability of notifications
- Ability to move with test product
- Subjects worry of leakage before and after use of test product
- Confidence to avoid full leakage with test product compared to only using usual product
- Confidence in daily life compared to only using usual product
- Feeling of control with test product compared to only using usual product
- Control of leakage progression with test product compared to only using usual product
- Feeling of security with test product compared to only using usual product
- Evaluation of confidence to increase social activities with test product compared to only using usual product
- Evaluation of sleep with test product compared to only using usual product
- Confidence at night with test product compared to only using usual product
- Evaluation of users' preference
- Reason for preference
- Evaluation of users' peace of mind with test product
- To evaluate users' assessment of QoL with test product compared to usual product
- Adhesive residue to transmitter

- Adhesive residue to skin

Explorative endpoints:

- Change in HRQoL, Appendix 1
- Change in Ostomy Leakage Impact (OLI), Appendix 2
- Evaluation of self-management (predictability of change) of stoma appliance compared to usual product

[redacted]

5.4. Rationale for selection and measurement of endpoints

The endpoint of system performance has been selected as primary endpoint in this investigation as this is the core performance measure of the system. The objective measure of leak notification accuracy (system performance) will be obtained by comparing leak areas from pictures of the backside of the adhesive baseplate to the output leak notifications received by the subjects for each of the leak sensor areas.

Secondary endpoints are related to users experience of reliability of leak notifications as well as users experience of what the product might offer them to support control, confidence and feeling of security in everyday life and whether it may help to reduce their worry of leakage, especially leakage onto clothes.

Secondary endpoints related to user experience with use of test product are asked on five-point Likert scales or as yes/no questions.

5.5. Demography and potential compromising factors

Assessments:

- Baseline/demographics
- Gender
- Age
- Weight
- Height
- Duration of ileostomy/colostomy (year when created)
- Reason for creation of the stoma
- Shape of the stoma
- Size of the stoma (diameter on widest place and height)
- Body profile
- Physical activity
- Sweat
- Output
- Information about the current stoma product
- Normal changing pattern
- Normal main reason for change of product
- Stoma awareness
- Technical ability
- Use of accessories
- Worry about leakage
- Reason for change (continuous)
- Wear time (continuous)

5.6. Equipment/methods and timing for assessing the variables

Assessment data will be captured at V1 by the study nurse who enter the data in the eCRF. Secondary and explorative endpoint data will be captured at V1 and V2, by the subject who will enter the data in the clinical trial app on the provided iPhone.

5.7. 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, applicable EC and regulatory authorities will be notified.

- First subject enrolled (04/2021).
- Last subject enrolled (05/2021).
- Last subject completed (06/2021).
- Final report (06/2022).

6. Clinical Investigation population

The clinical investigation will be conducted in 25 subjects enrolled from one clinical investigation site.

Due to the conceptual nature of this trial no formal sample size calculation has been performed. It is assumed that 25 subjects will be adequate for evaluating the sensor performance. Drop-out subjects will not be replaced.

We strive to include an equally number of users in the categories 1pc, 2pc, flat, convex and concave.

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

Inclusion criteria: 1. Have given written informed consent 2. Be at least 18 years of age and have full legal capacity 3. Have had a stoma for more than three months 4. Have intact skin on the area used in the evaluation meaning no broken skin and only minor discoloration of the skin (assessed by investigator) 5. Be able to use one of the five test products (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm) 6. Ileo- or colostomists with liquid output (Bristol scale type 6-7). 7. Currently using a Coloplast product (1pc/2pc Flat/Convex/Concave) from e.g Assura/SenSura/SenSura Mio 8. Have self-reported problems with leakage* (three times within 14 days) 9. Have worry of leakage 'to some, high or very high degree' 10. Is familiar with the use of a smartphone *Leakage: Leakage is defined as output from the stoma on the backside of the baseplate (underneath the baseplate)	Inclusion: 1. To meet the Helsinki Declaration 2. To meet the Helsinki Declaration 3. Recovered from ostomy surgery 4. The skin must be intact, otherwise the product will change classification category. 5. The technical design of the device requires use of one of the five sizes 6. The technical design of the device requires liquid output 7. To minimize unknown factors from competitor adhesives, only users of Coloplast products can be enrolled in this study. 8. The sensors in the product will only be activated by moist/leakage so in order to be able to evaluate the product the subjects need to have a certain amount of leakage. 9. Users who do not worry of leakage at any or low degree are excluded. 10. Users who do not know how to maneuver a smartphone will have to large difficulties in using the product and will also not be able to use the product going forward as it requires that the user has a smartphone.

6.1.2. Exclusion criteria

Exclusion criteria	Exclusion:
1. Currently receiving or have within the past 2 month received radio- and/or chemotherapy 2. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment. 3. Are pregnant or breastfeeding** 4. Participating in other interventional clinical investigations or have previously participated in this investigation. Exception: Participation in other Coloplast sponsored clinical investigations is accepted under the circumstances that the subject has paused the activities in the investigation and are otherwise complying with the inclusion and exclusion criteria of this protocol. 5. Known sensitivity towards test product 6. Known sensitivity towards acrylate 7. Is using/have a pacemaker 8. Is using ostomy paste or ostomy powder	1. The skin undergoes major changes because of radio- and/or chemotherapy, and therefore it can be more fragile to base plate changes 2. Steroid product may interfere with the study end points by making the peristomal skin thinner and more fragile 3. Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown 4. Other interventional investigation guidelines/products may interfere with these investigational endpoints. Some of the Coloplast studies are taking place over a two-year period, where the subjects will be paused for longer periods between the visits - therefore they are allowed to participate in other Coloplast studies meanwhile. 5. To protect subjects wellbeing 6. To protect the subjects from unnecessary harm 7. To protect the subjects from unnecessary harm users with a pacemaker are excluded 8. The use of ostomy paste or ostomy powder may influence system performance and is excluded in this study

** Besides a negative pregnancy test the women must also commit to use safe contraceptives during the study period (i.e. contraceptive coil, hormone base contraceptives or surgical sterilisation). However, in some cases when the women are older than 50 years, but are not yet post-menopausal, the investigator may evaluate that it is not reasonable to ask these women to start using safe contraceptives for the duration of the investigation (e.g. if the subject is abstinent, the partner is surgically sterilised, or either subject or partner is infertile). In these cases, the investigator can include the woman, but has a responsibility of ensuring that he/she has done what he/she can to prevent these subjects from becoming pregnant. As a minimum investigator must talk to the women about the risk of and how to avoid unwanted pregnancy at inclusion and at every visit hereafter.

Subjects who uses a mouldable ring may be included, if able to fit one of the five test products while wearing the ring. The sensor layer should be applied to the peristomal skin, not covering the ring.

6.2. Recruitment and enrolment

Recruitment of potential subjects will begin once approval have been obtained from the Ethics Committee and the Danish Medicines Agency

Recruitment method	[redacted]	**Advertisement**
Potential subjects	[redacted]	

	ileostomy or colostomy and be at least 18 years of age.	
First contact	[redacted]	Interested subject contact the investigator or delegated study personnel
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 informational 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 either remotely or in a room ensuring quiet surroundings. That could either be in the subject own home or at Coloplast if preferred by the subject. 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 **Error! Reference source not found.** 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 he/she 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.	

It is estimated that the recruitment process will be completed within 8 weeks.

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:

- 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.

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 18.

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 5.7

6.5. Subject Identification and Confidentiality

Subjects will be identified on the electronic CRF (eCRF) and any other document transmitted to the sponsor by the principal investigator or clinical site staff, 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 for each clinical investigation site will maintain as part of the investigational file a list identifying all subjects entered into the clinical investigation.

7. Procedures

7.1. Clinical investigation-related procedures

7.1.1. Visits

All visits (V) will be planned to be remote visits using Microsoft Teams, Skype or Face time, if technically possible. If a remote visit is not possible, a face to face meeting will be scheduled, either at subjects' own home or at Coloplast A/S, Humlebæk.

Visit 0 (Inclusion visit)
If a potential subject is interested in participating after the first contact and they met screening and inclusion criteria, a visit (visit 0) is arranged. 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. Hereafter, relevant female subjects will be asked to take a pregnancy test. 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 are allocated a subject number. Visit 0 and visit 1 can be combined.

Visits (V1)
During visit 1, baseline questions will be completed by the Principal Investigator, or delegate. The subject will be trained in the use of the clinical trial app, which is used for taking photos of used products at each product change, and how to complete the questions prompted at product change. The Principal Investigator, or delegate will ensure questions relevant for visit 1 are completed. At visit 1 the subjects will also thoroughly be trained in the use of the test product and instructed to continue their everyday life.

Visits (V2)
During visit 2, potential (S)AE's will be captured by the Principal Investigator, or delegate. During visit 2, the Principal Investigator, or delegate will ensure questions relevant for visit 2 are completed, hereafter termination.

Visits (Vx)
If circumstances demand it e.g. due to specific issues with the test product, an additional visit may be scheduled. In section 7.2 Flow-chart, assessment and endpoints are specified.

7.2. Flow-chart

Table 1 chart showing the connection between visits and assessments.

	Registration/measurement	PERFORMED BY	INFOR-MATION MEETING	SCREEN ING	VISIT 1	VISIT 2 TERMI-NA-TION	CON-TINOUS LY
	General						
	Oral information	Investigator	X				
	Written informed consent	Investigator	X	X			
	Check of in- and exclusion criteria	Investigator		X			
	Insurance of subjects' wellbeing and compli-ance with CIP	Investigator		X	X		
	Registration of Demographics/assess-ments						
	• Gender • Age • Weight • Height • Duration of ileostomy/colostomy (year when created) • Reason for creation of the stoma • Shape of the stoma • Size of the stoma (diameter on wid-est place and height) • Body profile • Physical activity • Sweat • Output • Information about the current stoma product • Normal changing pattern • Normal main reason for change of product • Stoma awareness • Technical ability • Use of accessories	Investigator			X		
	○ Wear time ○ Reason for change	Subject					X X

No.	Registration/measurement	PERFORMED BY	INFOR-MATION MEETING	SCREEN ING	VISIT 1	VISIT 2 TERMI-NA-TION	CON-TINOUS LY
	Primary endpoint						
1	To evaluate system performance focusing on accuracy of data classification into true positive and true negative	sponsor representative (evaluate pictures, assess leak to sensors) Subject (takes pictures at each change)					X
	Secondary endpoint(s)						
2	Frequency of leakage onto clothes	Subject			X	X	
3	Overall experience of leakage onto clothes with test product compared to only using usual product	Subject				X	
4	Reliability of notifications	Subject				X	
5	Ability to move with test product	Subject				X	
6	Subjects worry of leakage	Subject			X	X	
7	Confidence to avoid leakage onto clothes with test product compared to only using usual product	Subject				X	
8	Confidence in daily life compared to only using usual product	Subject				X	
9	Feeling of control with test product compared to only using usual product	Subject				X	
10	Control of leakage progression with test product compared to only using usual product	Subject				X	
11	Feeling of security with test product compared to only using usual product	Subject				X	
12	Evaluation of confidence to increase social activities with test product compared to only using usual product	Subject				X	
13	Evaluation of sleep with test product compared to only using usual product	Subject				X	
14	Confidence at night with test product compared to only using usual product	Subject				X	
15	Preference	Subject				X	
16	Reason for preference	Subject				X	
17	Evaluation of users' peace of mind with test product	Subject				X	
18	To evaluate users' assessment of QoL with test product compared to usual product	Subject				X	
19	Adhesive residue to skin	Subject				X	
20	Adhesive residue to transmitter	Subject				X	
	Exploratory endpoints						
Appx 1	HRQoL evaluation	Subject			X	X	
Appx 2	OLI evaluation	Subject			X	X	
21	Evaluation of self-management (predictability of change) of stoma appliance compared to usual product	Subject				X	

	Registration/measurement	PERFORMED BY	INFOR-MATION MEETING	SCREEN ING	VISIT 1	VISIT 2 TERMI-NA-TION	CON-TINOUS LY
22	[redacted]						
23							
	Registration of termination						
	AEs/ADEs/SAEs/SADEs	Investigator		X	X	X	X
	Termination form	Investigator					X

7.3. Case Report Forms

All assessments and observations throughout the investigation must be carefully recorded in an electronic CRF (eCRF), or an application (Clinical Trial App) in a provided phone for each subject. Details about data capture can be found in section 10.1

7.4. Concomitant treatment

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

7.5. 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 with access to CRFs
- Smartphone with Clinical Trial app.
- Nurse kits including disposal bags, gloves, gauze, disinfection gel etc.
- Tripod (a helping device to fixate the phone at virtual meetings)

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 animal testing.

All unacceptable risks related to the device have been mitigated as far as possible and have been deemed acceptable for the clinical study.

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

The investigation is conducted in accordance with current law and applicable standards, see section 15. Statement of Compliance. The rights, safety and well-being of human subjects shall prevail over the interest of science of society.

Risks in this investigation are considered to be equal to the use of ostomy products already on the market. Risks associated with the use of ostomy products are skin irritation and mechanical trauma. Please also see Adverse events, adverse device effects and device deficiencies section 18.

There is no known interaction between the use of the test product and the medication participants can take – except from what is stated in the exclusion criterions. Disadvantages of testing may be the time spent on visits and responding questions regarding product change.

There is no benefits for the subjects in this investigation, except the test products should be able to notify the subject if leakage occurs, which could be beneficial for the subjects in regards to the quality of life and maybe minimize the worry about leakage. The outcome of this investigation will contribute with important information for development of products for subjects with a stoma.

8.3. Delegation of responsibility

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.

9. Monitoring

The sponsor is responsible for ensuring appropriate monitoring of the clinical investigation activities as described below.

The monitor will be the primary contact for the principal investigator and clinical investigation site personnel.

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 site personnel in carrying out clinical investigations and specific study designs.

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

9.1.1. Site selection visit

Depending on the prospective clinical investigation 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 and common agreement between sponsor and principal investigator shall be reached. This visit may also be replaced by one or more phone calls if the principal investigator is known to the sponsor.

9.1.2. Initiation visit

The initiation visit will be held at Coloplast Holtedam 1, Humlebæk. At the initiation visit, study personal will get a full training on all aspects of the clinical investigation incl. the use of the Investigator Site File. The initiation visit will be held as close to study start as possible.

9.1.3. Monitoring visit(s)

The site dedicated monitor is to ensure adherence to the clinical investigation plan, accurate data recording on the e-CRFs and to monitor recruitment rates and adherence to follow-up schedules. 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 period of involvement for each clinical site personnel must be documented on the delegation log as well as training received before getting involved with the clinical investigation must be documented in the training log.

The monitor shall inform the sponsor about any problems relating to facilities, technical equipment or medical staff at the clinical investigation site. During the clinical investigation, monitors shall check that appropriate

written informed consents have been obtained. 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 in the monitoring plan.

The monitor shall make written reports to the sponsor, after each visit and provide written action items if any, to the principal investigator or clinical investigation site personnel.

All data collected can be directly entered into the eCRF and the EDC system will via edit checks ensure that all fields are completed in the eCRF. Monitor will ensure by 100% monitoring, that all queries are timely resolved.

Source data verification will be performed to the extent it is possible. The Source Data Specification Form must be completed at the initiation visit detailing the location of the source data for each data point. Where no source data (besides the eCRF) is available the contents of the eCRF will be monitored.

The Informed Consent Forms, Letter of Authority and AE/ADE will be 100% monitored for timely completeness.

Only the investigator, delegated site personnel and the sponsor representatives will have access to all the eCRFs.

9.2. Source data verification

A source document is a document in which data collected for a clinical trial is first recorded. This data is usually later entered in the electronic case report form (eCRF). Source documents are defined as "original documents, data, and records". Source documents contain source data, which is defined as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.

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 timeliness 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 eCRFs may be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. In most cases, the eCRF will 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.

10. Statistical considerations

10.1. Statistical design, method and analytical procedures

Definition of analysis populations

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

The ITT population (full analysis set) will be constituted by all included subjects who:

- Have provided valid informed consent
- Have information for at least one of the endpoints

The Safety population will constitute by subjects who have given informed consent.

All statistical analysis and summaries will be based upon the ITT population whereas adverse events and Device deficiencies will be assessed based on the safety population. Invalid individual data points may be omitted from analysis even though the corresponding subject is part of the ITT population. Any exclusion of data points will be documented.

A formal PP population is not planned due to the explorative nature of the investigation. Considering the data obtained it might however be considered to make additional explorative analyses based on a subset of the ITT population.

Analysis of endpoints, individual questions and baseline data
All endpoints and individual questions as well as baseline/demographic data will be listed and summarized by descriptive statistics. Summaries can be made for 1- and 2-piece users as well as for the subgroups (flat, convex and if relevant concave) or (IPhones, Androids), if relevant.
The accuracy of the sensor performance will be calculated based on picture data used to correlate notifications given with output to sensors on baseplates (primary endpoint). The accuracy will be calculated by dividing the true positive plus the true negative with the total sum of the true positive, true negative, false positive and false negative.

For secondary endpoints where the possible answer is Yes or No, the proportion of subjects answering "Yes" will be calculated. By use of an exact test in the Binomial distribution a 95% confidence interval will be estimated for the proportion. Further, it will be tested if the proportion is significantly different from 50% when using a 5% test level. For questions answered on a 5-point scale the answers can be grouped in 2 (e.g. "higher" or "much higher" against the rest of the answers) and analyzed by the above described method.

The total HRQoL score and the OLI sub scores will be analysed by a paired t-test to compare the results from Visit 1 (own product) and Visit 2 (own and test product).

The frequency of leakage on close before and after use of use of Olympus will be analysed by a Poisson loglinear model taken the paired design into consideration.

Users worry of leakage given on a 5-point scale will be analysed by a proportional odds ratio model taken the paired design into consideration to compare the results from Visit 1 (own product) and Visit 2 (own and test product)..

Other summaries and analyses can be made, if relevant.

As it is an exploratory study no adjustment for multiple testing will be applied.

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

10.2. Sample size
Due to the conceptual nature of this trial no formal sample size calculation has been performed. It is assumed that 25 subjects will be adequate for evaluating the sensor performance.

We strive to include an equally number of users in the categories 1pc, 2pc, flat, convex and concave.

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

10.3. 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.

10.4. Pass/fail criteria
No formal success criteria are applied in this investigation. Study results may be used for relevant claims.

The study will provide valuable insight into the performance and safety of the device and the ability to support the user with useful information regarding potential leakages in an everyday life setting.

10.5. Interim analysis

There is no planned interim analysis in this investigation that will affect the evaluation of the objectives. To facilitate and optimize the development of improved versions of the algorithm engineers working with the software will get restricted access to data before DBL. The result of their work will be for internal optimization of future versions of the algorithm only and will not be reported before after the result meeting of the study.

10.6. Statistical reason for termination of investigation

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

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

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

11. Data management

11.1. Data collection and data management

11.1.1. Data Collection in the clinical investigation

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 section 8

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.

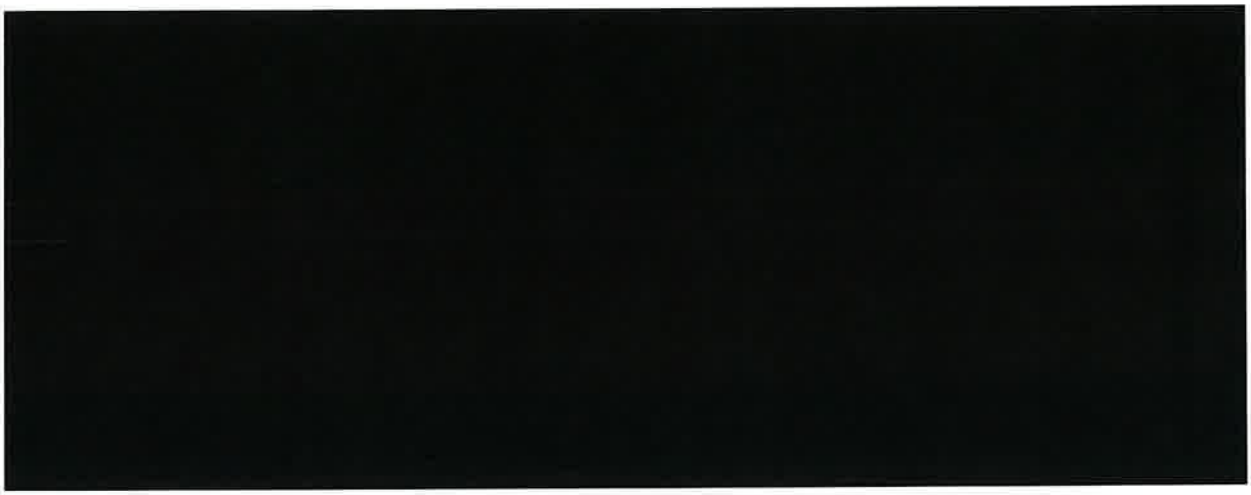
Principal Investigator, or delegate, at the clinical site will perform primary data collection directly into the eCRF or drawn from source-document (medical records) reviews. The eCRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up.

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 subject will receive a smartphone with the Clinical Trial app installed. The app is developed on behalf of Coloplast A/S [redacted]. This Clinical Trial app is used for taking photos of used products and used during the investigation every time the subject makes a product (1pc) or baseplate (2pc) change.

[redacted]



11.1.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The principal investigator or delegate 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.

11.2. 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 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 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

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

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/CA approved investigation plan. A minor deviation is defined as those that don't 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.

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 for all data-related deviations and all deviations that are **not** related to the data (for example, an untrained nurse performing study procedures). Deviations are reported in the Deviation Log located in the Investigator File.

If any deviations to the 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.

The following information about the deviation will be collected:

- Site ID, Subject ID
- Deviation Date and Investigation Visit
- Date deviation was discovered
- Clear and concise description of the event
- 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.

13.1. Violations to the Clinical Investigation Plan

Violations to the Clinical Investigation Plan occurs when there is major deviation from the EC approved investigation plan that also increase risk or decrease 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.

If any violations to the investigational plan are detected, the Investigator must inform the Monitor immediately, and the Monitor will complete an investigation specific Violation Form, enter it in the investigation deviation log (eCRF or Deviation Log in the Investigator File), and inform the Clinical Manager or designee immediately.

The Monitor must report all violations detected during a monitoring visit in the Periodic Monitoring Report.

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

- Date of receipt.
- Identification of each investigational device (batch no./serial no./unique code).
- 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.

15. 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 64th WMA General Assembly, Fortaleza, 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".
- Any applicable regional or national regulations will be specified in the country specific CIP.

15.1. Ethics committee and regulatory authorities

The CIP and/or other relevant documents are submitted to the appropriate EC(s) and regulatory authorities. This clinical investigation will not begin until the required approval from the EC and regulatory authorities have been obtained. Any amendment to the protocol will be submitted to the same EC(s) and regulatory authority.

Sponsor will notify the relevant regulatory authority and 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, in the event that 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: [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 the sponsor investigator agreement.

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 25 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 [redacted] per visit 1and 2, in total [redacted] if the subject completes the investigation

If the subjects are not able to conduct remote visits and do not want a home visit, the cost of transport between Coloplast A / S and the home will be covered. Reimbursement of transport expenses are not taxable whereas payment for participation in the study is taxable per local legislations. Subjects will be paid for their participation after each visit and transport expenses will be paid in appropriate portions that justify the administration, throughout investigation period.

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 and have a minimum of 24h before deciding on participation, but if the subject have decided to participate in the they can sign immediately. 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. The signature can be either in handwriting or by using an electronic signature form like DocuSign.

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. 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.

17. Subject compensation

17.1. Compensation in case of injury

Subjects will be covered through Coloplast insurance see 15.3

17.2. Compensation for participating in the clinical investigation

Subjects will be compensated as described under Financial conditions 15.4

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, 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.

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 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, deployment, implantation, installation and operation, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

Table 2 lists anticipated adverse device effects that may occur.

Table 2 Anticipated adverse device effects and their likely incidence rates

ANTICIPATED ADE	INCIDENCE RATE
Peristomal skin irritation (incl. mechanical trauma)	< 10%
Allergic peristomal skin irritation (dermatitis)	< 1%

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, safety or performance. This includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labelling.

Example: Transmitter not able to charge.

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 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.

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. 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. In this investigation no SADE are anticipated.

18.4.3. 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.

18.5. 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.

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 must be reported to sponsor within 10 days 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.
- **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:

[redacted] **and** [redacted]

18.8. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported to national competent authorities and ethics committees 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 national regulatory authorities.

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 relevant EC(s). 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 appropriate and notify the EC 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 on the subjects as necessary.

20. 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.

Clinical Manager has the responsibility to submit the approved clinical investigation report EC and regulatory authorities within a year after completion of the investigation.

21. Publication policy

Publication policy is specified in Sponsor Investigator Agreement.

21.1. General

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 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 CIP.

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

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

22. Bibliography

[1] Porret T et al. DialogueStudy: An international real-life study of stoma care nursing using a new ostomy appliance. Gastrointestinal Nursing. 2011 Mar 9(2) (Supplement): 1-24.

[2] Nybaek H, Knudsen DB, Laursen TN, Karlsmark T, and Jemec GB. Quality of life assessment among patients with peristomal skin disease. Eur J Gastroenterol Hepatol. 2010 Feb; 22(2): 139-43

[3] Clinical Investigation plan CP278, Doc. No: VV-0197006

[4] Clinical Investigation plan CP308, Doc. No: VV-0264003

[5] Intended Purpose - Olympus, Doc. No: VV- 0241767

[6] Product Description Olympus CP321, Doc. No: VV-0299255

[7] Product Composition Olympus CP321, Doc. No: VV-0299959

[8] Clinical Investigation Report CP278, Doc No: VV -0264051

[9] Clinical Investigation Device Label CP321, Doc. No: VV-0304934

[10] Biological Evaluation CP321, Doc. No: VV-0302274

[11] Investigators Brochure CP321, Doc No: VV-0309147

23. Appendix

23.1. Appendix 1 – Quality of life questionnaire

This questionnaire asks you about the use of the stoma appliance from this test period and your experiences. You will be asked questions about the discreetness of the stoma appliance, comfort relating to wearing the stoma appliance, confidence you have with the stoma appliance, and how the device impacts your social life.

Please think about your experience with using the stoma appliance **during the past seven days** and please select the box that is closest to your current situation. There are no right or wrong answers. We want to understand how beneficial you think the stoma appliance is and also what problems you may have experienced with it.

For each of the statements, think about how the specific issue affects you. Please answer **ALL** questions as honestly as you can, and **please remember to answer the questions in relation to the past seven days only.**

Discreetness 1. It was difficult to hide the stoma appliance under clothing 2. I was self-conscious about the appearance of the stoma appliance 3. The stoma appliance limited the choice of clothes that I could wear 4. The stoma appliance was obvious to other people 5. The color of the stoma appliance was discreet 6. It was difficult to hide the stoma appliance because of ballooning	**Confidence** 1. I was confident that the stoma appliance would not leak 2. I worried that the stoma appliance would become loose from my body 3. I felt confident that I could spend the night away from home despite wearing the stoma appliance 4. I was confident the stoma appliance would not cause any problems for me 5. I felt confident to take part in physical activities (for example, sports) whilst wearing the stoma appliance 6. I worried that the stoma appliance would make a rustling noise.
Comfort 1. The stoma appliance was comfortable to wear 2. I was not concerned about skin irritation under the stoma appliance (for example, feelings of burning, itching, pinching or pain) 3. It was uncomfortable to remove the stoma appliance from my body 4. I often forgot that I was wearing the stoma appliance 5. The stoma appliance was comfortable as it fitted well to my body 6. The stoma appliance disrupted my sleep during the night	**Social life** 1. I worried that my family and friends felt awkward around me because of the stoma appliance 2. I felt my social life had been restricted because of the stoma appliance 3. I avoided close physical contact with family and friends because of the stoma appliance 4. I worried about whether I could have a relationship because of my stoma appliance 5. I worried about whether the stoma appliance would affect my sex life

23.2. Appendix 2 – Leakage scale questionnaire (OLI)

Emotional impact

When you thought about your ostomy device and the risk of leakage, what emotions did you feel?

In the last 7 days, due to leakage or worry about leakage...	**All of the time**	**Often**	**Sometimes**	**Rarely or never**
1. I felt panic	0	1	2	3
2. I felt stressed out	0	1	2	3
3. I felt more afraid about leaks in the future	0	1	2	3
4. I felt worry	0	1	2	3
5. I felt frustrated	0	1	2	3
6. I felt embarrassed	0	1	2	3
7. I felt worried that I might leak	0	1	2	3
8. I couldn't sleep	0	1	2	3
9. I kept waking up at night to check my stoma	0	1	2	3
10. I kept checking my ostomy bag to see if I have leaked	0	1	2	3

Usual and Social activities

When you thought about your ostomy device and the risk of leakage, how did it affect your activities?

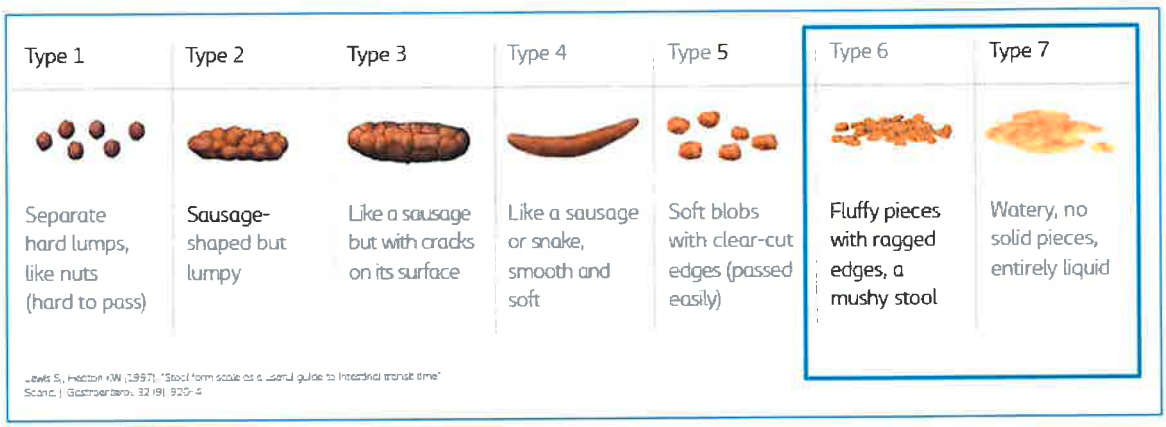
In the last 7 days due to leakage or worry about leakage...	**All of the time**	**Often**	**Sometimes**	**Rarely or never**	***Not applicable***
11. I decided to stay at home	0	1	2	3	9
12. I couldn't do light activities	0	1	2	3	9
13. I changed my plans	0	1	2	3	9
14. I was unable to go out and meet family and friends	0	1	2	3	9
15. I avoided close physical contact with family and friends	0	1	2	3	9
16. I did not want to see people	0	1	2	3	9
17. I avoided people	0	1	2	3	9
18. I tried to avoid meeting new people	0	1	2	3	9

Coping and in control

When you thought about your ostomy device and the risk of leakage, how did it affect your ability to cope?

In the last 7 days, due to leakage or worry about leakage...	**All of the time**	**Often**	**Sometimes**	**Rarely or never**
19. I felt in control	0	1	2	3
20. I was able to cope	0	1	2	3
21. I felt calm	0	1	2	3
22. I saw my friends as I usually do	0	1	2	3

23.3. Appendix 3 - Bristol scale



Lewis S., Heaton KW. (1997). "Stool form scale as a useful guide to intestinal transit time". Scand. J. Gastroenterol. 32 (9): 920–4.

23.4. Appendix 4 – Questions

Assessment/endpoint	Question	Answer
Assessment		
Reason for change	What is the reason for change? Please tick ALL that apply.	• I follow my usual changing pattern • There is leakage under and outside the baseplate (soiling the clothes) • Due to a notification from the App • The entire baseplate is detached • The outer edge of the baseplate is detached • The center of the baseplate is detached • I am afraid the baseplate will detach • The area around the stoma is itching • The area around the stoma is painful • There is leakage under the baseplate (but not outside the baseplate) • The stoma bag is filled with air • There is a vacuum in the stoma bag • Other
Secondary endpoint(s)		
Frequency of leakage onto clothes	Think back on the last 3 weeks - how many times have you experienced leakage unto clothes?	Number
Overall experience of leakage onto clothes with test product compared to only using usual product	Compared with your usual product, to which degree have you experienced leakage onto your clothes with test product?	Fewer episodes of leakage onto clothes - More episodes of leakage onto clothes
Reliability of notifications	To which degree did you find the notifications from the App reliable and trustworthy?	Very high degree - High degree - Some degree - Low degree - Not at all
Ability to move with test product	Compared to your usual product, how was your freedom to move with test product?	Much better - better - Same - Worse - Much worse
Users worry of leakage	Think back on the last 3 weeks - to which degree have you worried about leakage?	Very high degree - High degree - Some degree - Low degree - Very low degree/Not at all

Confidence to avoid leakage onto clothes with test product compared to only using usual product	Compared to your usual product, did you feel confident that you could avoid leakage onto clothes?	Yes – No
Confidence in daily life compared to only using usual product	Compared to your usual product, to which degree did the test product give you confidence in daily life?	Much higher degree- Higher degree- Same degree - Lower degree- Much lower degree
Feeling of control with test product compared to only using usual product	Compared to your usual product, did test product give you a feeling of leakage control?	Yes, higher leakage control No, lower leakage control
Control of leakage progression with test product compared to only using usual product	Compared to your usual product, did the test product give you a feeling of control of leakage progression?	Yes, higher control of leakage progression No, lower control of leakage progression
Feeling of security with test product compared to only using usual product	Compared to your usual product, did you feel more or less secure with test product?	I felt more secure – I felt less secure
Evaluation of confidence to increase social activities with test product compared to only using usual product	Compared with your usual product, did the test product affect your confidence to engage in social activities such as seeing friends, and do physical activities?	I felt more confident - I felt less confident
Evaluation of sleep with test product compared to only using usual product	Compared with your usual product, did the test product affect your sleep?	Yes, to the better Yes, to the worse No, the same
Confidence at night with test product compared to only using usual product	Compared with your usual product, to which degree did the test product give you confidence at night?	Much higher - Higher - Same - Lower - Much lower
Preference	Which product solution do you prefer?	Own product - Own product with test product
Reason for preference	What is your reason for preference? (Please tick all that apply)	• Body fit • Ability to bend and stretch • Feeling of security • Feeling of confidence • Less fear of leakage onto clothes

		• Discreet to wear • Discreetness in leakage control • Better sleep • Less embarrassment • Other text
Preference	How often would you use the test product?	Will never use it – Will use it rarely – Will use it sometimes – Will use it often – Will use it every day
Preference	If the test product was available today, would you start using it?	Yes – No
Preference	Would you recommend the product to others living with a stoma?	Yes – No
Evaluation of users' peace of mind with test product	To which degree did the test product give you peace of mind?	Very high degree- High degree- Low degree- Very low degree
To evaluate users' assessment of QoL with test product compared to usual product	Overall, do you think the test product can improve your feeling of control and confidence to avoid leakage onto clothes and therefore improve your quality of life?	Yes - No => if no, why not? Text
Adhesive residue to skin	To which degree did you experience adhesive residue to the skin in the area around the transmitter?	Very low degree/Not at all - Low degree - Some degree – High degree -Very high degree
Adhesive residue to transmitter	To which degree did you experience adhesive residue on the backside of the transmitter?	Very low degree/Not at all - Low degree - Some degree – High degree -Very high degree
Exploratory endpoints		
HRQoL evaluation		See Appendix 1
OLI evaluation		See Appendix 2

Evaluation of self-management (predictability of change) of stoma appliance compared to usual product	To which degree does test product support you to control the daily routines around appliance change?	Very high degree - High degree - Some degree - Low degree - Very low degree / Not at all
Evaluation of self-management (predictability of change) of stoma appliance compared to usual product	To which degree does test product make it easier to know when to change appliance compared to own product?	Very high degree - High degree - Some degree - Low degree - Very low degree / Not at all
[redacted]		

Signature Page for VV-0308987 v2.0

Approved	[redacted] 29-Mar-2021 12:03:16 GMT+0000
Approved	[redacted] 29-Mar-2021 13:35:22 GMT+0000
Approved	[redacted] 29-Mar-2021 13:39:23 GMT+0000
Approved	[redacted] 29-Mar-2021 14:56:10 GMT+0000

Signature Page for VV-0308987 v2.0

Document Owner: [redacted]