Clinical Investigation Plan

CP343

A randomized, controlled clinical investigation of an improved two-piece stoma product for people living with a stoma

Version 2.0, 14 October 2022

NCT05652010

CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

SYNOPSIS OF THE CLINICAL INVESTIGATION

Title
CP343: A randomized, controlled clinical investigation of an improved two-piece stoma product for people living with a stoma

Test Product and Comparator:

Test Product:

- SenSura Mio Click maxi bag (open, wide outlet), 50mm Ø with new coupling and lock ring
- Baseplate flat: SenSura Mio, click base plate with belt ears, 50 mm, 10-45 mm [redacted]
- Baseplate Concave: [redacted] SenSura Mio Concave, click base plate with ears size Ø50, 10-45 mm

Comparator:

- SenSura Mio Click 2p bag [redacted] Open, wide outlet, maxi, neutral grey. 50mm [redacted]
- Baseplate flat: [redacted] SenSura Mio Click Base Plate with belt ears, 50 mm, 10-45 mm
- Baseplate concave: [redacted] SenSura Mio Concave, click base plate with ears size Ø50, 10-45 mm

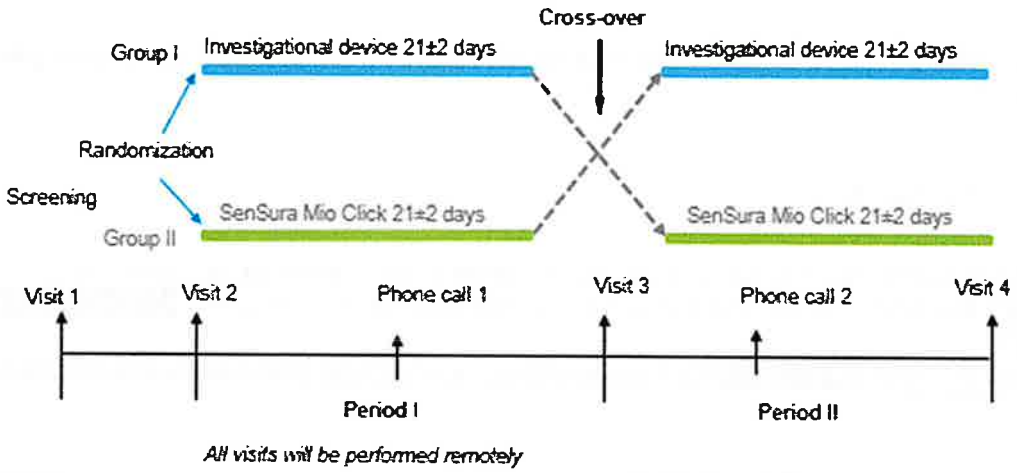
Objective(s)
The objective of the study is to investigate how a new two-piece (2p) coupling system performs in comparison with SenSura Mio Click regarding leakage at the coupling during wear (at each bag change) in a clinical setting.

Design of the investigation
Open-label, randomized, controlled, comparative, cross-over study with 2 test sequences comparing a new 2p coupling system with SenSura Mio Click. Each test period is 3 weeks (± 2 days), total study period is 6 weeks (± 4 days). It will be a 1:1 randomization into the two possible treatment sequences.

The investigation will require 50 randomized subjects (exp. 20% drop-out), leading to at least 40 completed subjects. The sample size calculation is based on at least 6 bag changes during each test period (≥2 changes per week).

All visits will be performed as remote virtual calls. At the visits, the investigator (or designee) will give instructions for the coming period and check that the trial is running as planned. At every bag change the subject will be asked to complete a questionnaire.

Cross-over design with two sequences



All visits will be performed remotely

A follow-up call will be scheduled 7±1 days after each test visit to ensure compliance with the provided product and study procedures. Additional calls may be scheduled if needed (assessed by the Principal Investigator or designee).

A subject is considered enrolled once consented. Screen failures are considered subjects who have consented, yet do not meet eligibility based on inclusion and/or exclusion criteria or withdraw consent prior to being randomized.

A subject can be randomized by mistake e.g., if the investigator realizes that the subject is not eligible after the subject has been randomized. If the subject has not started study treatment and has no data registered on endpoints the subject can be replaced by a new subject if the new subject can complete the investigation within timelines (before last subject last visit and within visit windows). A screen failure will be replaced under the same conditions.

Expected duration of the clinical investigation:

The investigation will be conducted from December 2022 through June 2023.

Endpoints & Assessments:

Primary Endpoint:

- Leakage through coupling registered at each bag change (yes/no).

Secondary endpoints:

- Product satisfaction evaluated at end of study by a question on a 4-point scale
- Preference evaluated at end of study by the question "Would you consider using the new coupling in the future? (Yes/No)"

Exploratory endpoint

[redacted]

Assessments

- Level of leakage at each bag change. If the subject responds as "yes"; the subject will be asked to grade the leakage on a 3-point scale.

[redacted]

Safety assessments:

- Adverse events
- Device deficiencies

Registered at the inclusion visit by Investigator or designee:

- Informed Consent
- Subject number
- Date of visit
- Check of inclusion criteria
- Check of exclusion criteria
- Current product (flat / concave, current bag size), item numbers (bag and baseplate)
- Name/type of randomized product

Baseline information and questions (registered at the inclusion visit by investigator or designee):

- Demographic (age, gender, height, weight)
- Stoma (age, type, cause, size, shape)
- For colostomy: Bristol stool scale
- Output frequency

Population/subjects

Subjects with an ileostomy or subjects with a colostomy with liquid fecal output, currently using the SenSura Mio Click 2p coupling (50mm Ø) with a flat or concave baseplate. The investigation will require 50 randomized subjects (expected 20% drop-out), leading to at least 40 completed subjects. Subjects will be enrolled through a single center[redacted].

Definition of liquid fecal output for subjects with a colostomy: Six or seven on the Bristol stool scale (Appendix 1)

Inclusion/Exclusion Criteria:

To be included in the investigation a subject must comply with the following inclusion criteria:
1. Has given written consent to participate by signing the Informed Consent Signature Form
2. Be at least 18 years of age and have full legal capacity
3. Is able to handle (apply, remove, cut, etc.) the product and do the assessments themselves
4. Has an ileostomy or colostomy with consistent liquid fecal output (for colostomy: 6-7 Bristol stool scale*) *See appendix 1
5. Currently use SenSura Mio Click 2p Click flat or concave with 50 mm coupling size
6. Have had their ostomy for at least 90 days
7. Be willing to change the bag at least twice per week
8. Is willing and suitable (determined by the Principal Investigator or designee) to use flat or concave 2p open product during the investigation
9. Is willing to use 2p maxi open bags during the investigation

A subject is excluded from the investigation in case he/she:
1. Is currently receiving or have within the past 60 days received radio-and/or chemotherapy - low doses radio- and/or chemotherapy (assessed by Principal Investigator) is allowed for indications other than cancer.

2.	**Is currently receiving or have within the past 30 days received topical steroid treatment in the peri-stomal skin area, e.g., lotion or spray** - **Low dose systemic steroid treatment (e.g., inhalation) assessed by the investigator are allowed.** - **Other systemic steroid treatment (e.g., injection or tablet) are not allowed.**
3.	**Is pregnant and/or breast-feeding**
4.	**Have a loop ileostomy**
5.	**Is currently using convex baseplate**
6.	**Has known hypersensitivity towards any of the products used in the investigation**

LIST OF ABBREVIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION *(IF APPLICABLE)*
ADE	Adverse Device Effect	See section 18.1
AE	Adverse Event	See section 18.0
ASADE	Anticipated Serious Adverse Device Effect	See section 18.5
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	
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
SAE	Serious Adverse Event	See section 18.3
USADE	Unanticipated Serious Adverse Device Effect	See section 18.6

SIGNATURE PAGE

All parties declare by their signature electronically on a separate signature page to follow the Clinical Investigation Plan CP343 in accordance with the Declaration of Helsinki, ISO 14155, and FDA Regulations.

> TABLE OF CONTENTS

1. List of personnel involved in the Investigation

1.0. Sponsor representatives

Coloplast A/S located at Holtedam 1-3; 3000 Humlebæk in Denmark is the Sponsor for this clinical investigation.

SENIOR CLINICAL MANAGER	PRINCIPAL BIOSTATISTICIAN
[redacted]	[redacted]
SENIOR SCIENTIFIC MANAGER	**SENIOR DATA MANAGEMENT SPECIALIST**
[redacted]	[redacted]

1.1. Site Personnel

This clinical investigation will be conducted in the United States at a single-center [redacted].

The Clinical Manager is responsible for maintaining an updated list of all sites and personnel in the sponsor electronic trial master file (eTMF). Qualified site personnel can perform investigational related tasks per the Principal Investigator's (PI) delegation. This delegation must be documented in the 'Site Personal Signature and Delegation List' for each site. All PIs and designees will receive training in all aspects of the investigation and before they can begin any study related procedures.

1.2. Clinical Research Organizations

A Site Management Organization (SMO) will be used to help conduct the investigation as a clinical site. All sponsor representatives' roles and responsibilities will be listed on the 'Site Personnel and Contact Details List'.

1.3. Other Vendors

The data management system is delivered by [redacted] The system is designed for electronic data capture, and it is compliant with the requirements of 21 CFR part 11.

The subject will be required to download and install a Patient Cloud app onto their smart phone. See section 11 for further details.

The app will be used to record subject diary responses.

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

2. Justification for conducting the clinical investigation

People with intestinal stomas have, despite development of better stoma products, problems with leakage induced peristomal skin complications which influence quality of life negatively[1,2]. Although, the primary cause of peristomal skin complications is leakage of ostomy effluents under the adhesive barrier[3,4], leakage could also occur from other parts of stoma devices, for example through the coupling in 2-piece stoma devices. Coloplast wants to apply a new coupling system with improved functionality for SenSura Mio users who use a 2-piece appliance. The justification for conducting this clinical investigation is to investigate that the new coupling system is on par with the existing coupling SenSura Mio Click system with regards to leakage at the coupling.

3. Objective(s) of the clinical investigation

The aim of the study is to investigate how a new two-piece (2p) coupling system is evaluated by users in comparison with SenSura Mio Click.

The primary objective is to demonstrate that the performance of the new 2p coupling system is comparable to SenSura Mio Click coupling with regards to leakage at the coupling during wear in a clinical setting.

The secondary objective is to evaluate product satisfaction and preference of the new two-piece (2p) coupling system by users in a clinical setting.

4. Investigational Products

4.0. Description of Test Product

The test product consists of the following:

- SenSura Mio Click maxi bag (open, wide outlet), 50mm Ø [redacted] with a new coupling and lock ring
- Baseplate flat: SenSura Mio, click base plate with belt ears, 50 mm, 10-45 mm [redacted].

[redacted]

- Baseplate concave: [redacted] SenSura Mio Concave, click base plate with ears size Ø50, 10-45 mm

4.1. Description of the comparator product(s)

The following comparator products will be used in this investigation:

- SenSura Mio Click 2p bag [redacted]. Open, wide outlet, maxi, neutral grey. 50mm [redacted]
- Baseplate flat: [redacted] SenSura Mio Click Base Plate with belt ears, 50 mm, 10-45 mm
- Baseplate concave: [redacted] SenSura Mio Concave, click base plate with ears size Ø50, 10-45mm

The comparator products are already on the market and will be used within the intended purpose in this clinical investigation.

4.2. Manufacturing

The Test Products and comparators will be manufactured at Coloplast A/S, Holtedam 1-3, 3050 Humlebæk, Denmark.

4.3. Identification and traceability of the device

All investigational products (test and comparator products) are labelled as per regulations and include "CAUTION – Investigational device. Limited by United States law to investigational use" on the label. The products are also identified with study number, product name/code, and item/lot number and accounted for through a master sponsor accountability log. Upon IRB approval, investigational products will be shipped to the principal investigator, or designee. Additionally, all investigational products will be accounted for and documented on a site accountability log. The receipt and disposition of all investigational products will be verified through monitoring. All unused products will be returned to Coloplast at the end of the study.

4.4. Intended use of the device in the clinical investigation

The test product is intended to support collection of output from a stoma and to provide a seal between the bag and baseplate.

4.5. Intended population for the device

The test product is indicated for use with surgically created ileostomies and colostomies with liquid fecal output. The product is indicated for adults currently using SenSura Mio Click 2p coupling (50mm Ø) open bags with flat or concave baseplate. Definition of liquid fecal output for subjects with a colostomy (6-7 on the Bristol stool scale - See Appendix 1)

4.6. Handling of the investigational device

The handling of the investigational products is described in detail in the Instruction for Use (IFU), which is included in all boxes with the products.

All site personnel will receive training by the sponsor and/or principal investigator in the handling and correct use of the investigational products. The Principal Investigator, or designee, will train the subjects in the correct use of the investigational products.

For further details regarding the test product, please refer to the Investigators Brochure.

4.7. Total number of devices intended for the clinical investigation

The subjects will be included for $21^{+/-}2$ days per test period, for approximately 42 days.

Subjects are expected to change their products at least twice a week, but may change more frequently, and as frequently as once a day. Therefore, it is estimated subjects may use approximately 21 test product baseplates and 21 comparator baseplates during their participation. Subjects will be supplied with enough baseplates and bags for the duration of the investigation.

[redacted]

5. Design of the clinical investigation

5.0. General

This investigation is an open-label, randomized, controlled, comparative, cross-over study with 2 test periods and 2 test sequences comparing a new 2p coupling system with SenSura Mio Click. Each test period is 21 days (± 2 days). Each subject will participate for a total of 42 days (± 4 days). The subjects will test the investigational product and the comparator in a 1:1 randomised order. A total of 50 subjects will be enrolled and

randomized to yield 40 subjects (assuming a 20% drop-out rate) who complete the study. The sample size calculation is based on at least 6 bag changes during each test period (≥2 changes per week).

If a potential subject is interested in participating after the first contact, a visit (visit 0) will be arranged.

The subject 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. During the visit, the Principal Investigator or designee will provide oral information about the investigation based on the Subject Information Form.

Before the test periods, the subjects are invited for a screening visit (V1). Subjects will be consented prior to any study procedures. Once consented, during their participation, the subjects will complete three study visits (V2, V3 and V4). The visits will be done remotely via video conference. A follow-up call will be scheduled 7±3 days after each test visit to ensure compliance with the provided product and study procedures. Additional calls may be scheduled if needed (assessed by the Principal Investigator or designee).

At every bag change the subject will be asked to complete a questionnaire via an app installed on their smartphone.

During the visits the subject will complete a questionnaire and discuss any adverse events or device deficiencies they may have had with the site personnel.

Coloplast will provide both the investigational product and the comparator product for all subjects.

If a subject experience a problem with the investigational product during the investigation, he/she should contact the investigator for advice. Subjects that cannot complete a test period with the test product may choose to use their own product (i.e., SenSura® Mio) for the remainder of the test period. However, this must be documented by the Principal Investigator.

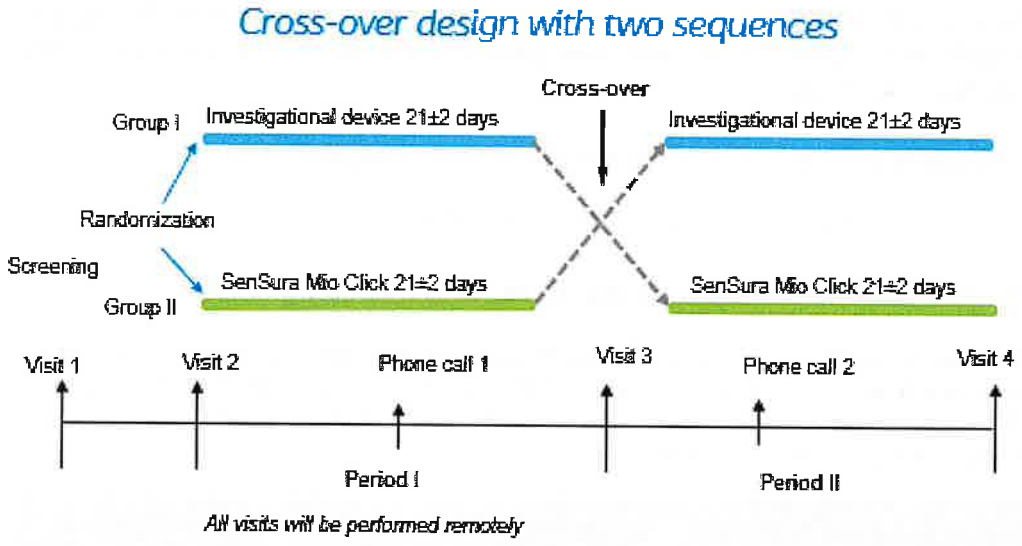


Figure 1 Design of the investigation.

5.1. Primary endpoint

The primary endpoint is leakage through coupling registered at each bag change. This is a yes/no response from the subject.

5.2. Secondary endpoints

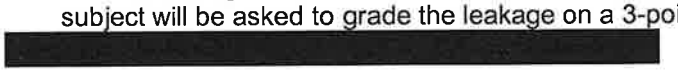
The secondary endpoints are as follows:

- Product satisfaction evaluated at end of study by a question on a 4-point scale
- Preference evaluated at end of study by the question "Would you consider using the new coupling in the future? (Yes/No)"

5.3. Exploratory endpoint

5.4. Assessments

- Level of leakage at each bag change. If the subject responds as "yes" for the primary endpoint; the subject will be asked to grade the leakage on a 3-point scale.



5.5. Safety Assessments

- Adverse events
- Device deficiencies

See appendix 2 for questions used as basis for the above endpoints and assessments.

5.6. Rationale for selection and measurement of endpoints

The primary objective is to investigate the performance of a new 2p coupling in comparison with the SenSura Mio Click coupling with regards to leakage at the coupling during wear in a clinical setting. For this reason, leakage at the coupling is chosen as primary endpoint. The secondary endpoints will inform about the general satisfaction with the new coupling.

5.7. Demography and potential compromising factors

The subjects are not allowed to currently (upon inclusion) receive or have within the past 60 days received radio-and/or chemotherapy. However, low doses radio- and/or chemotherapy (assessed by Principal Investigator or designee) is allowed for indications other than cancer.

The subjects are not allowed to currently receive or have within the past 30 days received topical steroid treatment in the peristomal skin area, e.g., lotion or spray.

The subject shall use the test and comparator product as they normally would use their standard care product. Subjects are allowed to use all the accessories they normally use with their own product, such as paste, protection film, lotion, powder, and remover wipes/spray.

5.8. Randomisation Procedure

All subjects that meet the inclusion and exclusion criteria will be randomised to one of two treatment sequences. Both sequences examine the investigational product and the comparator investigational product. The two sequences are:

- First sequence: The investigational product, then the comparator investigational products.

- Second sequence: The comparator investigational product, then the investigational product.

Randomization will be centralized using [redacted]

5.9. Blinding

No blinding will be used in this investigation, as it is not possible to blind the products due to visible differences. The trial statistician will be blinded until database lock to ensure decisions related to data before database lock do not affect the final results.

5.10. 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 regulatory authorities will be notified.

First subject enrolled (February 2023).

Last subject enrolled (April 2023).

Last subject completed (May/June 2023).

Final report (December 2023).

Subject participation will be approximately 42 days.

6. Clinical Investigation population

According to the sample size calculations (see section 10.2) 40 subjects are required to complete the study with measurements of the primary endpoint in both test periods. Considering a drop-out rate of 20%, the required total number of subjects to be enrolled in the trial shall be 50.

6.0. Eligibility criteria

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

6.1. Inclusion criteria

To be included in the investigation a subject must comply with the following inclusion criteria:
1. **Has given written consent to participate by signing the Informed Consent Signature Form**
2. **Be at least 18 years of age and have full legal capacity**
3. **Is able to handle (apply, remove, cut, etc.) the product and do the assessments themselves**
4. **Has an ileostomy or colostomy with consistent liquid fecal output (for colostomy: 6-7 Bristol stool scale*)** *See appendix 1
5. **Currently use SenSura Mio Click 2p Click flat or concave with 50 mm coupling size**
6. **Have had their ostomy for at least 90 days**
7. **Be willing to change the bag at least twice per week**
8. **Is willing and suitable (determined by the Principal Investigator or designee) to use flat or concave 2p open product during the investigation**
9. **Is willing to use 2p maxi open bags during the investigation**

6.2. Exclusion criteria

To be included in the investigation a subject must NOT meet the following exclusion criteria:
1. **Is currently receiving or have within the past 60 days received radio-and/or chemotherapy** - **low doses radio- and/or chemotherapy (assessed by Principal Investigator) is allowed for indications other than cancer.**
2. **Is currently receiving or have within the past 30 days received topical steroid treatment in the peristomal skin area, e.g., lotion or spray** - **Low dose systemic steroid treatment (e.g., inhalation) assessed by the investigator are allowed.** - **Other systemic steroid treatment (e.g., injection or tablet) are not allowed.**
3. **Is pregnant and/or breast-feeding**
4. **Have a loop ileostomy**
5. **Is currently using convex baseplate**
6. **Has known hypersensitivity towards any of the products used in the investigation**

6.3 Subject Recruitment & Screening

The recruitment of potential subjects will commence only when IRB approval is received. Recruitment will occur in the United States at the single-center [redacted] The recruitment period from first subject enrolled to last subject enrolled will be approximately 3 months. The recruitment process will be conducted through site screening and advertisement.

If a subject is eligible and interested in participating, then written information about the investigation (subject information) will be sent to the subject to ensure they are given the opportunity to understand what the investigation is about. Subjects will be given plenty of time to have any questions they may have addressed by the investigator, or designee. The subject information provides information to subjects about how to contact the investigator or a representative thereof, or a representative of the sponsor (name, telephone number and e-mail address), if they wish to learn more about the study.

If an eligible subject is interested in participating after they have had time to review the subject information, a screening visit will be arranged. This visit will be done remotely to ensure privacy for the subject. When arranging the visit, the subject must have received the Information Form and given adequate time to review it. The subject will receive both written and verbal information about the possibility of allowing a companion to the remote visit and to any possible subsequent remote visits.

The subject has the right to wait before deciding to participate. If/when the subject decides to participate, he/she will be asked to sign the informed consent form. 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 subject is considered enrolled in the investigation.

The Coloplast clinical manager will have close contact to the site during the recruitment period. The principal investigator, or designee, will notify the clinical manager when a subject is enrolled and all future planned visits.

6.4 Point of enrolment

A subject is considered enrolled in the investigation at the time of consent. Prior to any clinical investigation-related procedures are undertaken, the subject signs and dates the informed consent form. The expected duration for each subject is described in section 5.10.

6.5 Subject Screening and randomization Failures

Subjects that have signed the informed consent form but fail to comply with the eligibility criteria are considered screening failures. A screening failure will be replaced by a new subject if the new subject can complete the investigation within timelines (before last subject last visit and within visit windows).

Screen failures are also considered subjects who have consented but withdraw consent prior to being randomized.

In rare cases, randomization errors can occur, and subjects are randomized by mistake, e.g., if the investigator realizes that the subject is not eligible after the subject has been randomized. In these cases, if the subject has not started study treatment and has no data registered on endpoints; the subject can be replaced by a new subject if the new subject can complete the investigation within timelines (before last subject last visit and within visit windows).

If a subject is randomized to one test sequence but by mistake gets products for the opposite sequence it will be regarded as a randomization failure. As this is an exploratory investigation the statistical analyses will in that case be based on the actual test sequence and not the randomized sequence

6.6 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. If, after these attempts are made, and there is still no response, the subject will be withdrawn from the clinical investigation

6.7 Subject Identification and Confidentiality

Subjects will be identified on the electronic CRF (e-CRF) and any other document transmitted to the sponsor by the principal investigator or clinical site staff, by a unique identification number.

Data entered on the e-CRF are confidential and will only be available to the sponsor (including sponsor delegates), members of data management teams, the statistician, data monitoring board members or clinical event committee members if involved, members of the EC or IRB 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

7.0. Clinical investigation-related procedures

Before initiation of the clinical investigation, Coloplast must be provided with key personnel signed and dated curricula vitae (not more than two years old) to verify qualifications. Key site personnel are those, who treat or evaluate subject data in the clinical investigation. Coloplast will ensure that all site personnel are trained in the investigation procedures, completion of the eCRFs, procedure for reporting a device deficiency, an adverse event or serious adverse event (how, when, to whom), and who to contact in case of emergency related to the investigational products.

See section 7.3for an overview of the clinical investigation-related procedures during subject visits, telephone visits, and at each bag change.

7.1. Subject Visits

Visit 0 - Screening (Day 0)

If a potential subject is interested in participating after the first contact, a visit (visit 0) will be arranged. When arranging the visit, it will be ensured, that the subject has received the Subject Information Form and given

plenty of time to review it. The subject 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 any subsequent visits. During the visit, the Principal Investigator or designee will provide oral information about the investigation based on the Subject Information Form. The subject has the right to wait before deciding on participation.

Visit 1 – Inclusion (Day 1)

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 informed consent form has been signed, the subject is considered enrolled in the investigation. Enrolled subjects are entered in the electronic data capture system and will be randomised to either the test product or comparator . If a subject is enrolled and does not meet inclusion/exclusion criteria, they will be deemed screen failures and will not be randomized.

Once the subject has consented, the investigator and/or delegated site personnel will conduct the following:

- The investigator/study nurse will re-review study procedures.
- Subject is allocated a subject number
- Verification of inclusion/exclusion criteria
- Randomization (including subject number & name/type of randomized product)
- Collection of baseline data
    - Demographics (age, gender, height, and weight)
    - Current product (flat/concave, bag size, item numbers)
    - Stoma (age, type, cause, size, shape)
    - Bristol scale score (Appendix 1)
    - Output frequency

- Shipment of investigational products to subject

Visit 2 – Start of first test period (Day 3 + 2 days)

- Study Personnel will review App with subject and collect safety data, if applicable.
- First application of investigational product – test product OR comparator (Day 1 of Test period 1)

Test period 1:

- Testing test product / comparator product for 21 ± 2 days
- Telephone Visit at Day 7±1 after application of product/comparator:
    - Investigator/study nurse must call the subject to ensure that the subject is compliant with:
        - Study procedures and
        - Completion of subject diary
- Diary completion at every bag change
- Adverse Events, if applicable
- Device Deficiencies, if applicable
- Protocol Deviations, if applicable

Visit 3 - Cross-over Visit (Day 25 ± 2 days)

- Subject will be contacted by investigator/study nurse to review procedure for cross-over
- Study Personnel will review compliance with subject and collect safety data, if applicable. Application of investigational product - test product OR comparator (Day 1 of Test period 2)
- Adverse Events, if applicable
- Device Deficiencies, if applicable
- Protocol Deviations, if applicable

Test period 2:

- Testing test product / comparator product for 21 ± 2 days
- Telephone Visit at Day 7±1 after application of product/comparator:
    - Investigator/study nurse must call the subject to ensure that the subject is compliant with:
        - Study procedures and
        - Completion of subject diary
- Diary completion at every bag change
- Adverse Events, if applicable
- Device Deficiencies, if applicable
- Protocol Deviations, if applicable

Visit 4 – Completion/Termination (Day 46 ± 2 days)

- Subject will be contacted by investigator/study nurse for study completion or termination
- Study Personnel will review compliance with subject and collect safety data, if applicable.

NOTE:

1. *See Appendix 2 for details on the subject questions included in the subject diary. The subject diary will be provided to the subjects using an app installed on their smart phones.*

2. *Subjects who are unable to complete a test period may move forward to the next visit and test period instead of dropping out of the investigation.*

7.2. Safety Follow up:

Adverse events and device deficiencies will be assessed at all visits, planned and unplanned. Subjects are followed through termination of the investigation (Visit 4). Any ongoing ADEs or SADEs at study termination will be followed until resolution. All subjects are encouraged to contact the Principal Investigator, or designee, if they experience problems that they believe are related to their investigational product or participation. This is to ensure that any device-related events are documented and to safeguard the subjects' health.

7.3. Schedule of Assessments

Table 1- Study assessments.

	PERFORMED BY	VISIT 1	VISIT 2	VISIT 3	VISIT 4
Informed consent (Allocation of Subject Number in EDC)	Investigator/Delegated Site Personnel	X			
Inclusion/Exclusion criteria	Investigator/Delegated Site Personnel	X			
Shipment of investigational products	Investigator/Delegated Site Personnel	X			
Randomization	Investigator/Delegated Site Personnel	X			
Baseline Data Collected	Investigator/Delegated Site Personnel	X			
Application of device (test product or comparator)	Subject		X	X	
Questionnaire completed at each bag change during test period 1 & 2	Subject		X	X	
Final evaluation questionnaire completed at end of study					X
Ensure Compliance	Investigator/Delegated Site Personnel		X	X	X
Telephone Call	Investigator/Delegated Site Personnel		(Day 7 of test period 1)	(Day 7 of test period 2	
Protocol Deviations, If applicable	Investigator/Delegated Site Personnel	X	X	X	X
Adverse Events, if applicable	Investigator/Delegated Site Personnel	X	X	X	X
Device Deficiency, if applicable	Investigator/Delegated Site Personnel		X	X	X

7.4. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in an electronic CRF (eCRF).

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

Subjects will be asked to complete a questionnaire at every bag change. The questionnaire will be completed on a clinical trial app which will be downloaded onto their smart phones.

It is the responsibility of the Investigator that all data are entered promptly and correctly.

8. Risk – benefit analysis and ethical considerations

8.0. Risk-benefit analysis of the investigational device

[redacted]

This clinical study is performed to confirm that the new coupling is on par with SenSura click with regards to leakage at the coupling.

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, and laboratory testing.

The risk management process has been performed in accordance with the requirements stated in ISO 14971:2012 and in accordance with internal Coloplast procedures, including design verification, validated test methods, risk analysis and completion of a biological evaluation report for the test product.

To mitigate and reduce the risks, the site personnel will be trained, according to the IFU.

The investigation is conducted in accordance with current applicable standards. Please refer to section 15.0, Statement of compliance. The rights, safety and well-being of human subjects shall prevail over the interest of science.

Risks have been proven minimized or eliminated through appropriate design control, confirmed by pre-clinical bench, and laboratory studies.

8.1. 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.

The participating subjects will contribute with important information for the development of a new coupling. Due to the actions taken to mitigate any risks, the risks and disadvantages when participating in this clinical investigation are estimated as low. The subject's health will not benefit directly from this investigation.

8.2. Risk Analysis for the conduct of the clinical investigation

A risk assessment of the clinical investigation will be conducted initially prior to the first subject enrolment and periodically re-assessed based on any new risks identified through the process. This assessment will be completed throughout the duration of the investigation, as defined by the study team.

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. A study-specific monitoring plan has been developed and includes details regarding the monitoring strategy (i.e., on-site, remote, and centralized).

The monitors 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 extent 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 this clinical investigation, the below described monitoring procedures have been determined.

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

The monitoring will be conducted per the monitoring plan by qualified designee personnel.

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

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

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

- Site selection visit
- Site Initiation Visit
- Periodic Monitoring visits
- Close Out visit

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.

Initiation visit

All clinical investigation sites will complete an initiation visit during which full training on all aspects of the clinical investigation will be provided.

Monitoring visit(s)

The site dedicated monitor is to ensure adherence to the clinical investigation plan, the safety of the subjects, accurate data recording on the e-CRFs and to monitor recruitment rates and adherence to follow-up schedules. During the clinical investigation, monitors shall check that appropriate written informed consents have been obtained. The principal investigator shall permit and assist the monitor to carry out verification of completed e-CRFs 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 Site Personnel signature and Delegation list as well as training received before getting involved with the clinical investigation must be documented in the Clinical Investigation Training Log.

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

The sponsor, or delegate, will provide clinical monitoring, including review of eCRF with verification to the source documentation, as defined in the monitoring plan. The monitor shall make written reports to the sponsor, including documentation of any deviations after each visit and provide written follow up action items if any, to the principal investigator and/or clinical investigation site personnel.

Periodic monitoring visits (remote or on-site) will be performed as soon as reasonable possible, after the site has enrolled the first subject in the investigation. A final monitoring visit will be performed after all subjects on site have completed the investigation.

A remote, centralized review of the data entered in the eCRF, will be performed by Coloplast CM throughout the conduct of the investigation.

9.1. Source data verification

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

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

10. Statistical considerations

10.0. Statistical design, method, and analytical procedures

The primary objective will be evaluated by analysis of the primary endpoint [redacted]. The secondary objective will be evaluated by analysis of the secondary endpoints.

All baseline measurements, endpoints and assessments will be summarized by descriptive statistics and/or listed. Endpoints and assessments will be summarized by product. 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.

Other summaries can be made, if relevant. As it is an exploratory study no adjustment for multiple testing will be applied.

All statistical analysis and summaries will be performed with SAS (version 9.4/Enterprise Guide version 7.1)

Definition of analysis populations

Intention to Treat (ITT) and Safety populations will be defined at a formal data review meeting 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 with valid informed consent who have been exposed to at least one product, with information on at least one product with respect to the primary endpoint or the secondary endpoints.

Any exclusion of subjects from the ITT population must be documented. 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.

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

All statistical analysis will be based upon the ITT population whereas adverse events and device deficiencies will be assessed based on the safety population.

Considering the data obtained it might be considered to make additional explorative analyses based on a subset of the ITT population.

Analysis of the primary endpoint
The leakage (Y/N) per bag change will be analyzed by a repeated logistic regression model. The model will consider that observations corresponding to different subjects are independent, whereas observations corresponding to the same subject are correlated. The correlation between observations corresponding to the same product can be larger than observations corresponding to different products. Hence the model includes a fixed effect of product (SenSura Mio, test product), a fixed period effect, a random effect of subject and a random interaction effect of product and subject.

The marginal proportion of leakage for two products will be estimated and it will be tested if the odds ratio is significantly different from 1 on a 5% test level.

Analysis of the secondary endpoints
For preference, 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 4-point scale the answers will be grouped in 2 (e.g., "Very satisfied" or "Satisfied", represented by "Yes" against "Very dissatisfied" and "Dissatisfied" represented by "No") and analysed using the method described above.

Analysis of the exploratory endpoint
[redacted]

[redacted]

10.1. Sample size
The primary objective is to investigate the performance of a new 2p coupling in comparison with the SenSura Mio Click coupling with regards to leakage at the coupling during wear in a clinical setting. This will be done by testing if the odds ratio for the estimated proportions of leakage with the two products is equal to one.

[redacted]

Drop-out subjects will not be replaced but to account for an assumed drop-out rate of 20%, 50 subjects will be randomized in the study.

10.2. Level of significance and power
A two-sided significant level of 5% will be applied. For a description of the power see section 10.2 above

10.3. Pass/fail criteria
The purpose of the investigation is fulfilled:

- if the estimated proportion of leakage from the new coupling system is not statistically significant different from the current SenSura Mio 2p Click solution,
- or the estimated difference is not clinically relevant worse.

10.4. Interim analysis

There is no planned interim analysis in this investigation.

10.5. Statistical reason for termination of investigation

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

10.6. 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

11.0. Data collection and data management

Data Collection in the clinical investigation

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

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

The EDC system used [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 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.

In addition, an electronic patient-reported outcome (ePRO) app that collects subject responses to questionnaires/diaries and transfers data to the [redacted] Clinical Cloud will be used in this investigation. The subject will be required to download and install the Patient Cloud app onto their smart phone.

This Patient Cloud app is used during the investigation every time the subject makes a bag (2pc) change.

The ePRO used is [redacted] All data will be transferred automatically into the eCRF. If for some reason the app is not available before FPI the patient reported outcome questionnaires will be reported by using a paper diary which will be handed out to all subjects.

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.

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.

11.1. Remote monitoring

Remote (source data verification) and/or centralized (data review) monitoring is 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 (evaluation without visiting the investigation site). 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 e-CRF 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 deviations 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 deviations, and delays in reporting data), and clinical data to identify early on corrective actions needed for characteristics correlated with poor performance or noncompliance

11.2. Data retention

All investigation site documents must be archived for a minimum period of 10 years after the final clinical investigation report has been signed. The monitor is responsible for informing the investigator and the CM if this period should be longer for their sites according to local regulation.

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 IRB and applicable regulatory authority. Substantial changes may require approval from the IRB and applicable regulatory authority prior to implementation.

13. Deviations from the Clinical Investigation Plan

Deviations to the Clinical Investigation Plan occurs when the activities during the clinical investigation do not comply with the IRB and 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. If a deviation increases risk or decreases benefit and/or; has a significant effect on the subject's rights, safety, or welfare and/or has a significant effect on the integrity of the data it is defined as a major deviation and the Investigator must inform the monitor immediately, and the Monitor will report and inform the Clinical Manager or designee immediately.

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

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

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

If any deviations to the 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 IRB notification date, when applicable, and retrieve a copy of the IRB Submission Letter for the TMF.

14. Device Accountability

All access to the investigational devices (including comparators) 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./lot no.).
- Number of products received
- Number of products distributed to subject
- The expiry date, if applicable.
- The date(s) of use.
- Subject identification.
- The date on which the investigational device was returned/explanted from the subject, if applicable.
- The date of return unused, expired or malfunctioning investigational devices, if applicable.

15. Statement of compliance

The clinical investigation is conducted in accordance with:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Brazil, October 2013.
- FDA Regulations
- ISO 14155:2020 "Clinical Investigation of medical devices for human subjects – Good clinical practices".

15.0. Ethics committee and regulatory authorities

The CIP and/or other relevant documents are submitted to the appropriate IRB, if applicable. This clinical investigation will not begin until the required approval from the IRB has been obtained. Any amendment to the clinical investigation plan will be submitted to the same IRB. Sponsor will notify the relevant IRB of the end of the clinical investigation.

15.1. 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

15.2. Indemnity

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

15.3. Financial conditions

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

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 ensure ample time is provided before deciding on participation. The subjects will be informed that their participation is voluntary and that they may leave the investigation at any time, without this having any influence on their further treatment.

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

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

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

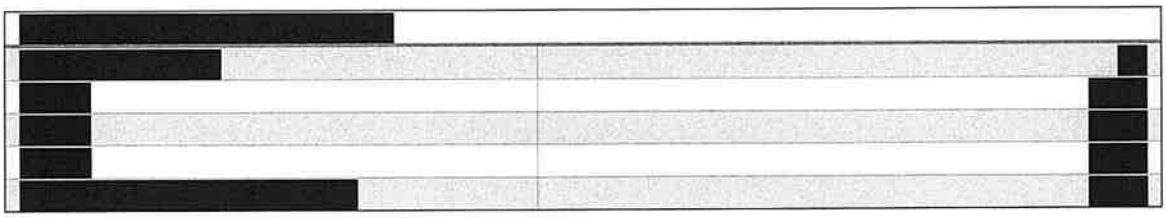
17.0. Compensation in case of injury

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

17.1. Compensation for participating in the clinical investigation

If applicable, subjects will be compensated for their participation in the clinical investigation.

Table 1 Example Compensation for subject participation



18. Adverse events, adverse device effects and device deficiencies

18.0. Adverse events

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

18.1. Adverse device effect

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

The definition of an adverse device effect includes any event resulting from insufficiencies or inadequacies in the instruction for use, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

18.2. Device deficiency

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

18.3. Serious adverse events (SAE)

A serious adverse event is an adverse event that:

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

- Led to foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment.

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

1) Suitable action had not been taken, or
2) Intervention had not been made, or
3) 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. 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.

18.5. Anticipated serious adverse device effect (ASADE)

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

18.6. 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.

18.7. Medical care of subjects

Principal investigator shall ensure that adequate medical care is provided, during and after participation in the clinical investigation, to a subject experiencing an adverse event. All ongoing ADEs, SAEs, SADEs and DDs that could have led to a SAE at subject termination will be followed until resolution. An ongoing adverse event at subject termination visit is documented as the current status for the adverse event and will not be followed up.

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

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

18.8. Reporting and timelines

18.9. Investigator's reporting responsibilities

PI at each site must assess all (S)AE`s that occur at his/her site.

- All serious adverse events and serious adverse device effects must be reported to sponsor within 24 hours of the site becoming aware of the event.

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

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

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

The investigator will assess intensity for each AE and SAE reported during the investigation and assign it to one of the following categories:

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

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

Please report to:

[redacted] Sr. Clinical Manager
[redacted]
[redacted]

and [redacted]

18.10. Sponsors reporting responsibilities

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

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

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

18.11. Medical Advisor Safety Review

The Sponsor is responsible for ensuring all Serious Adverse Event (s) are provided to the Medical Advisor for review and discussion.

The Medical Advisor will be informed of the following:

- All serious adverse events related to the investigation product or clinical investigation and serious adverse device effects
- 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
- New findings and/or updates in relation to already reported serious events

In addition, the Medical Advisor will receive lists of any reported AE's and ADE's related to the investigation product or clinical investigation, as defined by sponsor for a review of safety.

Correspondence, decisions, and recommendations regarding safety in the Clinical Investigation from the Medical Advisor must be documented and saved electronically in the Sponsor File.

18.12. Data Safety and Monitoring Board (DSMB)

The review of all safety data will be conducted on an ongoing basis to identify any potential safety issues. If needed, the Medical Advisor can call for a Data Safety and Monitoring Board meeting with relevant members, to discuss potential safety issues and further recommendations, if relevant.

Based on the safety data review, the Medical Advisor along with the DSMB may recommend that the sponsor modifies, temporarily suspends, or terminates the clinical investigation.

Correspondence, decisions, and recommendations regarding safety in the Clinical Investigation from the Data Safety and Monitoring Board must be documented in meeting minutes and saved electronically in the Sponsor File.

All final decisions, however, regarding clinical investigation modifications, remain with the Sponsor.

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 IRB. If monitoring or auditing of the clinical investigation identifies serious or repeated deviations at one of the participating investigation sites, sponsor will suspend or terminate the particular investigational site. The sponsor or investigator will inform the IRB as appropriate 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.

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.

The clinical investigation report must be submitted to the IRB.

21. Publication policy

The investigation will be registered at www.clinicaltrials.gov and results will be published on the same web page. No other publication is planned.

22. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if

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

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

23. Bibliography

1. Porret T et al. Dialogue Study: 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. Gray M, Colwell JC, Doughty D, Goldberg M, Hoeflok J, Manson A, McNichol L, Rao S: Peristomal moisture-associated skin damage in adults with fecal ostomies: a comprehensive review and consensus. J Wound Ostomy Continence Nurse 2013, 40(4):389-399.

3. Martins L, Samai O, Fernández A, Urquhart M, Hansen AS: Maintaining healthy skin around an ostomy: peristomal skin disorders and self-assessment. Gastrointestinal Nursing 2011, 9(Sup2):9-13

4. [redacted]

24. Appendix

Appendix 1: **Bristol stool scale.**

Only to be used for subjects with a colostomy. Subjects with a colostomy need to have liquid faecal output (type 6-7 on the Bristol stool scale).

Type 1	Type 2	Type 3	Type 4	Type 5	Type 6	Type 7
						
Separate hard lumps, like nuts (hard to pass)	Sausage-shaped but lumpy	Like a sausage but with cracks on its surface	Like a sausage or snake, smooth and soft	Soft blobs with clear-cut edges (passed easily)	Fluffy pieces with ragged edges, a mushy stool	Watery, no solid pieces, entirely liquid

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

Appendix 2 – Instructions & Subject Questionnaire

The participants must be instructed in the following:

- Bag change frequency: Bags must be changed at least twice per week. Baseplates can be changed at bag change or left until next change as they choose. They are welcome to change more than twice per week. If baseplate is changed, the bag should also be changed.
- It is very important to explain to the participants what is meant by "feces having leaked out *through* the coupling" not to be confused with leakage from under baseplate that has spread to the coupling from the outside.
- Explain how to scrutinize the coupling before changing the bag. Look at it from all sides (with help of a mirror and/or smartphone where not visible to the eye). Drawings will be helpful for explaining what to look for.
- Be careful to instruct that at bag change, the coupling on the baseplate must be cleaned thoroughly so leakage of feces during wear time is not confused with feces not having been cleaned from the coupling at bag change.
- Make sure to check that the coupling is clean after bag change.
- If both bag and baseplate are changed at the same time, it is ok to take them off together as we do not ask questions related to opening of the coupling.
- Make sure participants are guided on remembering in which test period (1 or 2) they tested the new coupling when the final questions are asked at visit 3.

Overall procedure at every bag change:

- Look at the coupling from all angles before changing any of the products
- Change the bag (or bag and baseplate)
- If only a bag change is performed - remember to check that the coupling is clean after the change
- Register date and time in the app.
- Answer the questions in the app.

Questionnaire at each bag change:

- Are there any signs of feces having leaked through the coupling since last bag change? (yes/no), IF YES: How much leakage through the coupling has there been? Please choose one of the options below:

1. Small
2. Medium
3. Large

Note: Subjects will be provided with examples as reference. (Refer to appendix 3)

- Did you use any supporting accessories (yes/no) If yes, click for options (multiple choice):

1. Paste
2. Elastic barrier strips
3. Protective film
4. Deodorant
5. Adhesive remover
6. Cleanser for the skin
7. Tape around the outer edge of the adhesive
8. Moldable rings/seals
9. Belt
10. Powder
11. Skin care lotion
12. Hernia belt
13. Supporting garment
14. Other, please specify_____

- Did you change the baseplate in addition to the bag change? (Yes/no)

Additional questions at Visit 4 or at Study Termination:

(Before answering the following questions, please clarify together with your study nurse which test period you tested the new coupling)

The new coupling was tested in (The first test period/the second test period) *(Click for options (only one):*

How satisfied are you with the new coupling? (Click for options (only one):

1. Very satisfied
2. Satisfied
3. Dissatisfies
4. Very dissatisfied

Would you consider using the new coupling in the future? (Yes/No)

Appendix 3 – Examples of Leakage at Coupling