Clinical Investigation Plan

CP338

The ATTRACT-I Study - **A** randomized con**T**rolled clinical inves**T**i-gation evaluating a flat ostomy bar**R**ier with [redacted]

NCT number: NCT04868617, Document approval date: 20 June 2021

[redacted]

CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	Initial document created based on template 9.0
2.0	[redacted]	Updates to section 5.6 and the statistical analysis sections 10.1.1 and 10.1.2 in response to the [redacted] request. In section 15.2, text has been changed from anonymized to pseudonymized
3.0	[redacted]	Additional revisions to section 10.1.2 in response to the [redacted] clarifying the primary endpoint analysis.

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[redacted]

SYNOPSIS OF THE CLINICAL INVESTIGATION

Title

CP338 / The ATTRACT-I Study - **A** Randomized Con**T**rolled Clinical Inves**T**igation Evaluating a Flat Ostomy Bar**R**ier with [redacted]

Test Product and Comparator:

The CP338 Coloplast investigational products are a non-CE marked stoma test product based on the [redacted] and [redacted] products which are comprised of a [redacted]

The comparator products [redacted] are considered Standard of Care.

Intended Purpose

The test product is intended to support collection of output from a stoma and to provide [redacted] The test product is indicated for use with surgically created ileostomies and colostomies with liquid fecal output.

Aim and Objective(s)

The **aim** of this investigation is to evaluate the performance and safety of [redacted]

The primary objective is to investigate whether [redacted] can reduce peristomal skin complications compared [redacted]

The secondary objective is to evaluate whether [redacted] can improve health-related quality of life of people with an ileostomy or colostomy with liquid fecal output.

Design of the investigation

This investigation is a randomized, controlled, open-label, comparative, cross-over, multicenter investigation, with two test periods. In total, 82 subjects will be included and randomized, and each subject will have three test visits overseen by the Principal Investigator, or designee. Each subject will be enrolled for $2 \times 35^{-1/+3}$ days in total for the entire investigation, thus approximately 70 days. The subjects will test the non-CE marked test product and the comparator product in randomized order.

Expected duration of the clinical investigation:

The investigation will be conducted from September 2021 through February 2022.

Endpoints & Assessments:

Primary endpoint:

- Peristomal skin condition measured by the Decision Tree Score on baseplate level at steady state (scale from 0-3) *Appendix 1*.

Secondary endpoint:

- Health-related quality of life measured by the DLQI score evaluated at the end of each test period (scale from 0-30) *Appendix 2*.

Exploratory endpoints:

[redacted]

[redacted]

Safety assessments:

- Adverse events
- Device deficiencies
- Concomitant medications

See appendix 3 for questions used as basis for the above endpoints and assessments.

Population/subjects

Subjects with an ileostomy or colostomy with liquid fecal output, currently using a flat baseplate. To take a potential drop-out (20%) into account it is recommended to include a total of 41 1-piece and 41 2-piece users, resulting in a total of 82 subjects included and randomized. The subjects will be included by competitive recruitment in up to 10 sites in five different countries (UK, Germany, Sweden, Norway, and Denmark).

Inclusion/Exclusion Criteria:

To be included in the investigation a subject must comply with the following inclusion criteria:	Justification for inclusion criteria
Has given written consent to participate by signing the Informed Consent Signature Form	To ensure that the subject has been given written and oral information regarding the investigation and know enough about the investigation to decide on participation.
Is at least 18 years of age and have full legal capacity	To meet the Helsinki Declaration
Has an ileostomy or colostomy with consistent liquid fecal output (6-7 Bristol scale*). *See appendix 6.	The product is indicated for use with ileostomies and colostomies with liquid fecal output.
Is currently using a [redacted] product with open bag.	The test products [redacted]
Has had the ostomy for at least 90 days.	To ensure that the initial post-operative problems are overcome, and that the subject is used to having an ostomy as well as changing the product before entering the investigation.
Can use an ostomy product with a max cut size of 45 mm (1-piece) or 38 mm (2-piece).	To accommodate the max cut sizes of the test products.

[redacted]

Has experienced leakage under the baseplate at least three times within the last fourteen days.** **Leakage defined as output/seeping under the baseplate (see appendix 7)	To ensure that the user has potential leakage induced skin complications.
Has experienced symptoms of peristomal skin complications such as itching, burning, or pain in the peristomal area within the last fourteen days. ** ** Proper training of the PI and nurses in how to ask the subject about these symptoms is essential.	To ensure that the user has skin complications in the peristomal area.
Is able to handle the electronic diary (questionnaire/photo) themselves. If needed, a trained spouse or caretaker is allowed to assist.	To answer the CRF questions and take pictures the subjects must be able to handle the electronic diary themselves. Or alternatively with assistance by a trained spouse or caretaker.
Is able to handle (apply, remove, cut, etc.) the product themselves.	To test the products at home, the subject must be able to handle the product themselves.
Understands that any barrier products (film, cream, spray, wipes etc.) are not permissible during the investigation, and is willing to not use these accessories during the investigation.	The use of any barrier products (film, cream, spray, wipes etc) could compromise the effect of the new baseplate.
Is willing and suitable (determined by the Principal Investigator or designee) to use [redacted] product during the investigation.	To ensure compliance with the protocol during the investigation.
Is willing to change the product (1-piece) or baseplate (2-piece) at least every fourth days.	To ensure enough changes is recorded in the CRF.

A subject is not allowed to participate in case he/she:	Justification for exclusion criteria:
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 other indications than cancer.**	The skin undergoes major changes because of radio- and/or chemotherapy, and therefore, the skin might be more fragile to product changes.
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.**	Steroid product on peristomal skin may interfere with the skin condition. Use of steroid product can make the skin more fragile to baseplate change.
Is breastfeeding.	Even though the ingredients and the recipes have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
Is pregnant based on urine pregnancy test.	Even though the ingredients and the recipes have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
Has known hypersensitivity towards any of the products used in the investigation.	It is not ethical to include persons that know they are allergic to the products used in the investigation and it would also create bias, as these persons would give the product they are allergic to a more negative rating and most likely also create an AE.

Investigation approval

The investigation will be approved by the competent authorities and ethical committees in the participating countries (The United Kingdom, Germany, Sweden, Norway, and Denmark) before investigation initiation.

[redacted]

LIST OF ABBREVIATIONS

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 18.4.2
CIP	Clinical Investigation Plan	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection
CM	Clinical Manager	
DD	Device deficiency	
EC	Ethics Committee	
eCRF	Electronic Case Report Form	
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 section 18.4.3

SIGNATURE PAGE

All parties declare by their signature on the electronic or the separate signature page to follow the Clinical Investigation Plan CP338 in accordance with the Declaration of Helsinki, ISO 14155 and the Medical Device Directive/Medical Device Regulation.

[redacted]

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[redacted]

1. List of personnel involved in the Investigation

1.1. Sponsor Representatives

Coloplast A/S, Holtedam 1-3, 3000 Humlebæk is the Sponsor in this clinical investigation.

LEAD CLINICAL MANAGER	STATISTICIAN
[redacted]	[redacted]
CLINICAL MANAGER	**DATA MANAGER**
[redacted]	[redacted]
MEDICAL WRITER	**PROJECT MANAGER**
[redacted]	[redacted]
MEDICAL ADVISOR	**DIRECTOR OF CLINICAL OPERATIONS**
[redacted]	[redacted]

1.2. Site Personnel

This clinical investigation involves up to 10 sites in five different countries: United Kingdom, Germany, Sweden, Norway, and Denmark.

The Clinical Manager is responsible for maintaining an updated list of all PIs, investigational sites, and institutions in the sponsor 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.

1.3. Clinical Research Organizations

Clinical Research Organizations (CROs) and Site Management Organizations (SMOs) will be used to help conduct the investigation as Sponsor representatives in one or more countries. All sponsor representatives' roles and responsibilities will be listed on the 'Site Personnel and Contact Details List'.

1.4. Other Vendors

The data management system is delivered by [redacted] and is named [redacted]. Current version number is version 2020 3.2. The system is designed for electronic data capture, and it is compliant with the requirements of 21 CFR part 11.

A clinical trial application (app) installed on an iPhone will be used in this investigation. The app is developed on behalf of Coloplast A/S by the development company [redacted]. The app will be used to record patient reported outcome data and photographs.

Discolouration and leakage area will be measured for each photograph by automated image analysis which will be conducted using an artificial intelligence programme developed by [redacted]

2. Rationale 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]. In fact, the primary cause of peristomal skin complication development is due to leakage of ostomy effluents under the adhesive barrier[3,4]. Some of the common clinical signs of peristomal skin complications include pain, itching, burning, discoloration, bleeding, and wounds[5]. To overcome this, Coloplast A/S has developed [redacted]

3. Objective(s) of the clinical investigation

The aim of this investigation is to evaluate the performance and safety of [redacted]

The primary objective is to investigate whether an [redacted] can reduce peristomal skin complications compared [redacted]

The secondary objective is to evaluate whether [redacted] can improve health-related quality of life of people with an ileostomy or colostomy with liquid fecal output.

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[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] 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.

[4] 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

[5] Voegeli, D., et al., Factors influencing the incidence of peristomal skin complications: evidence from a multinational survey on living with a stoma. Gastrointestinal Nursing, 2020. 18(Sup4): p. S31-S38.

4. Investigational Products

4.1. Description of Test Product

[redacted]

4.2. Comparator

[redacted]

4.3. Manufacturing

The non-CE marked Test Products will be manufactured at Coloplast A/S, [redacted]

The CE-marked comparators are manufactured by Coloplast A/S.

4.4. Identification and traceability of the investigational products

All investigational products (non-CE marked test products and [redacted]mparator products) are labelled as per regulations and include "Exclusively for Clinical 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 EC 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 though monitoring. All unused products will be returned to Coloplast at the conclusion of the study.

4.5. Intended use of the test product in the clinical investigation

The non-CE marked test product is intended to support collection of output from a stoma[redacted]

4.6. Intended population for the test product

The test product is indicated for use with surgically created ileostomies and colostomies with liquid fecal output. The product is indicated for adults.

4.7. Handling of the investigational products

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. It is stated in the IFU that the investigational products are for single-use and must be stored horizontally under dry and not freezing conditions and should be kept away from direct sunlight. Reprocessing, washing, disinfection, and sterilisation may compromise product characteristics, causing additional risk of physical harm to or infection of the user.

All Principal Investigators, and designees 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.

4.8. Total number of investigational products intended for the clinical investigation

The subjects will be included for 35 $^{-1/+3}$ days per test period, for approximately 70 days.

Subjects using 1-piece products are expected to change their products every day. Therefore, they are expected to use approximately 35 test products and 35 comparator products during their participation.

Subjects using 2-piece products are expected to change their products every two-three days. Therefore, they are expected to use approximately 20 test product baseplates and 20 comparator baseplates during their participation. Subjects using 2-piece products will be supplied with enough bags for the duration of the investigation.

5. Design of the clinical investigation

5.1. General

This investigation is a randomised, controlled, open-label, comparative, cross-over, multicentre investigation, with two test periods. In total 82 subjects will be included and randomised, and each subject will have at least three test visits overseen by the Principal Investigator, or designee. Each subject will be enrolled for 2 × 35 $^{-1/+3}$ days; thus approximately 70 days. The subjects will test the non-CE marked investigational product and the comparator product in a randomised order.

Before the test periods, the subjects are invited for a screening visit (V0). Subjects will be consented prior to any study procedures. Once consented, during their participation, the subjects will complete three study visits (V1, V2 and V3). The visits can be at the Principal Investigators clinic or in the subject's home. In rare cases (i.e., global pandemic), visits can be done remotely via video conference. In addition, the Principal Investigator, or designee, will call the subjects four times during the course of the investigation to inquire if the subject has had any issues or concerns.

During the test visits the subject will complete a quality of life questionnaire and discuss/record any adverse events or device deficiencies. The subject will also be asked about the use and handling of the product, and their preference.

At every baseplate change the subjects will be asked to take photos of their stoma/peristomal skin and the backside (adhesive side) of the used product. The photos will be taken with a smartphone using the Coloplast Clinical Trial App. The subject will also be asked to complete a questionnaire about their peristomal skin condition.

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

If a subject experiences 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. [redacted]) for the remainder of the test period. However, this must be documented by the Principal Investigator.

[redacted]

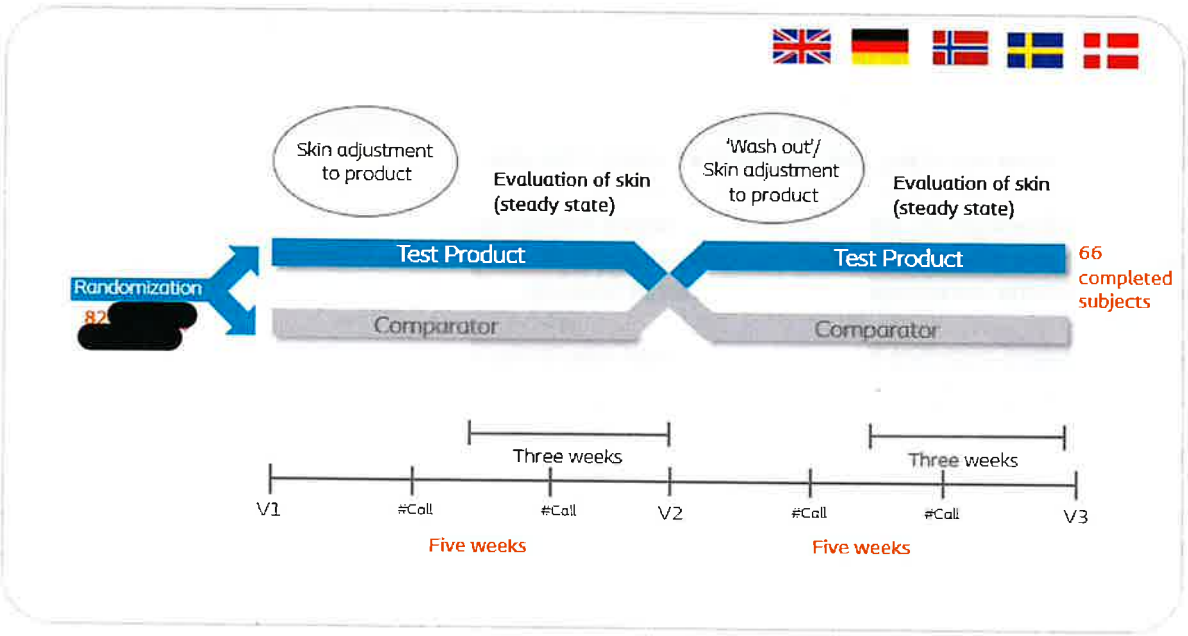

Figure 1: Trial Design

The duration of the test periods (35 $^{-1/+3}$ days) and number of visits should be adequate to assess data on the skin condition of the subjects. The investigational products are tested for 35 $^{-1/+3}$ days in each study period to ensure that the skin will have time to adjust to new conditions, reach a steady state, and for the subjects to test the product for an adequate number of days to give a thorough evaluation of the products.

To account for a possible carry-over effect, the steady state period of the treatment period begins after two weeks of product use. It is anticipated that the skin will have adapted to the new product after two weeks.

5.2. Investigation Endpoints

Endpoint details and flow-chart of measurements are presented in the appendices.

5.2.1. Primary endpoint

The primary endpoint is the peristomal skin condition measured by the Decision Tree Score on baseplate level at steady state (scale from 0-3). See appendix 1.

5.2.2. Secondary endpoint

The Secondary endpoint is a health-related quality of life measured by the (DLQI) score evaluated at the end of each test period (scale from 0-30). See appendix 2.

5.2.3. Exploratory endpoints:

[redacted]

[redacted]

Safety assessments:

- Adverse events
- Device deficiencies
- Concomitant medication

See appendix 3 for questions used as basis for the above endpoints and assessments.

5.3. Rationale for selection and measurement of endpoints

The primary endpoint as well as [redacted]ndpoints are subjective and objective parameters assessing the condition of the peristomal skin; and are essential to investigate whether the [redacted] can reduce peristomal skin complications induced by leakage of fecal output.

To evaluate the performance of the test product, the Decision Tree score will be applied. This score is the outcome of a modified version of the Ostomy Skin Tool 1.0.[6] The new skin tool, referred to as Ostomy Skin Tool 2.0 (manuscript in preparation), is comprised of a patient-reported outcome (PRO) questionnaire and an automated image analysis conducted via an artificial intelligence algorithm[7]. The PRO consists of six items designed to assess the severity of peristomal skin complications (appendix 4). The Decision Tree score captures both visual and non-visual signs of peristomal skin complications and assigns patients to a skin severity level based on the observed combination of these variables as outlined in appendix 1. The Decision Tree score successfully underwent a psychometric validation process; thereby, concluding that the Decision Tree score is a valid and reliable method for evaluating the peristomal skin condition in clinical trials (manuscript in preparation).

The Dermatology Life Quality Index (DLQI) will be used in this investigation (appendix 2) and is a validated, dermatology specific quality of life tool. The subject will complete a paper version of the DLQI at each study visit for the purpose of evaluating their health-related quality of life during each study period.

[redacted] and the possible effect [redacted] the [redacted]

Adverse events and device deficiencies will be collected to ensure safety.

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[6] Martins, L., et al., *The ostomy skin tool: tracking peristomal skin changes.* Br J Nurs, 2010. **19**(15): p. 960, 932-4.

[7] Andersen, N.K., et al., *Automated Assessment of Peristomal Skin Discoloration and Leakage Area Using Artificial Intelligence.* Frontiers in Artificial Intelligence, 2020. **3**(72).

5.4. Demography and potential compromising factors

The following baseline data will be collected and registered at the screening visit (V0) by the investigator or designee:

- Date of Informed Consent
- Subject number
- Date of visit
- Check of inclusion criteria
- Check of exclusion criteria
- Complete randomization

Please refer to Appendix 5 for the complete list of baseline data to be collected for each subject.

The subjects are not allowed to use barrier products (film, cream, spray, wipes etc.) during the investigation.

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. However, low dose systemic steroid treatment (e.g., inhalation) assessed by the Principal Investigator or designee is allowed. Other systemic steroid treatments (e.g., injection or tablet) are not allowed.

5.5. Equipment

Subjects will be supplied with an iPhone for the sole purpose of recording their daily product changes, completing questionnaires, and taking pictures of their stoma and used products. This data will be collected through the Clinical Trial application downloaded onto an iPhone. This iPhone must be returned to the investigator, or designee, upon study termination.

Subjects will use the clinical trial app at each product/baseplate change and at all study visits. Please refer to section 7.

5.6. Randomisation Procedure

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

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

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

Randomization will be centralized using [redacted]

5.7. 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 final results.

5.8. Total expected duration of the clinical investigation

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

- First subject enrolled (September 2021).
- Last subject enrolled (December 2021).

[redacted]

- Last subject completed (February 2022).
- Final report (August 2022).

Subject participation will be approximately 70 days.

6. Clinical Investigation population

According to the sample size calculations (see section 10.2) 66 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 82. The subjects will be enrolled in up to 10 clinical investigation sites and the aim is an equal split between 1- and 2-piece users.

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

To be included in the investigation a subject must comply with the following inclusion criteria:	Justification for inclusion criteria
Has given written consent to participate by signing the Informed Consent Signature Form	To ensure that the subject has been given written and oral information regarding the investigation and know enough about the investigation to decide on participation.
Is at least 18 years of age and have full legal capacity	To meet the Helsinki Declaration
Has an ileostomy or colostomy with consistent liquid fecal output (6-7 Bristol scale*). *See appendix 6.	The product is indicated for use with ileostomies and colostomies with liquid fecal output.
Is currently using a [redacted]product with open bag.	The test products [redacted]
Has had the ostomy for at least 90 days.	To ensure that the initial post-operative problems are overcome, and that the subject is used to having an ostomy as well as changing the product before entering the investigation.
Can use an ostomy product [redacted]	To accommodate the max cut sizes of the test products.
Has experienced leakage under the baseplate at least three times within the last fourteen days.** **Leakage is defined as output/seeping under the baseplate (see appendix 7)	To ensure that the user has potential leakage induced skin complications.

Has experienced symptoms of peristomal skin complications such as itching, burning, or pain in the peristomal area within the last fourteen days. ** ** Proper training of the PI and nurses in how to ask the subject about these symptoms is essential.	To ensure that the user has skin complications in the peristomal area.
Is able to handle the electronic diary (questionnaire/photo) themselves. If needed, a trained spouse or caretaker is allowed to assist.	To answer the CRF questions and take pictures the subjects must be able to handle the electronic diary themselves. Or alternatively with assistance by a trained spouse or caretaker.
Is able to handle (apply, remove, cut, etc.) the product themselves.	To test the products at home, the subject must be able to handle the product themselves.
Understands that any barrier products (film, cream, spray, wipes etc.) are not permissible during the investigation, and is willing to not use these accessories during the investigation.	The use of any barrier products (film, cream, spray, wipes etc) could compromise the effect of the new baseplate.
Is willing and suitable (determined by the Principal Investigator or designee) to use [redacted] during the investigation.	To ensure compliance with the protocol during the investigation.
Is willing to change the product (1-piece) or baseplate (2-piece) at least every fourth days.	To ensure enough changes is recorded in the CRF.

6.1.2. Exclusion criteria

A subject is not allowed to participate in case he/she:	Justification for exclusion criteria:
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 other indications than cancer.**	The skin undergoes major changes because of radio- and/or chemotherapy, and therefore, the skin might be more fragile to product changes.
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.**	Steroid product on peristomal skin may interfere with the skin condition. Use of steroid product can make the skin more fragile to baseplate change.
Is breastfeeding.	Even though the [redacted] have been approved for humans, their effect on embryos, foetuses, and infants are unknown.

Is pregnant based on urine pregnancy test.	Even though [redacted] have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
Has known hypersensitivity towards any of the products used in the investigation.	It is not ethical to include persons that know they are allergic to the products used in the investigation and it would also create bias, as these persons would give the product, they are allergic to a more negative rating and most likely also create an AE.

6.1.3. Pregnancy and breastfeeding

For female subjects with childbearing potential (they have had at least one period during the last 12 months), a urine pregnancy test will be performed at the inclusion visit, to ensure the subject is not pregnant. The urine pregnancy test will be performed by dipstick at the trial site. Furthermore, the female subjects should not be breastfeeding, when participating in the clinical investigation.

6.2. Subject Recruitment & Screening

The recruitment of potential subjects will commence only once authorisation has been received from the Regulatory Authorities (if applicable) and respective EC approval. Recruitment will occur through competitive enrollment in five countries: UK, Germany, Sweden, Norway, and Denmark. The recruitment period from first subject enrolled to last subject enrolled will be approximately four months. The recruitment process will be conducted through site screening and advertisement.

Advertisement will target local Coloplast consumer databases and online social media. The advertisement will state the contact information of relevant Principal Investigator(s) to contact or the web-address for a Coloplast 'recruitment landing page'. CROs will assist by receiving reply letters/mails and/or answering the phone from interested subjects.

Recruitment from hospitals, home care nurses and outpatient stoma clinics will be via patient screening visits or subject records kept at the participating sites.

6.2.1. Screening Potential Subjects

If a subject is eligible and interested in participating, then written information about the investigation (subject information) will be provided 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 can be done remotely or in a quiet room reserved to ensure privacy at the investigator's clinic/office. When arranging the visit, the subject must have received the Information Form prior to the visit and given adequate time to review it. The subject will receive both written and verbal information about the possibility of bringing a companion to the visit and to any possible subsequent 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 relevant forms. 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 each site during the recruitment period. The principal investigator, or designee, at each site will notify the clinical manager when a subject is enrolled and all future planned visits.

Sites will be instructed to recruit equal amounts of 1-piece and 2-piece users to the best of their ability. Once one of the respective groups is fully enrolled (i.e., 41 subjects); that groups recruitment will be paused in order to complete recruitment in the other group. When the Coloplast clinical manager is aware 82 subjects have been included and randomised, the recruitment will stop. If, at this time, there are subjects who have been informed of the investigation and are reflecting on participation, they will be given the opportunity to be included within the first 24 hours hereafter.

6.3. Point of Enrollment

A subject is considered enrolled in the investigation when written informed consent is obtained. The expected duration for each subject is described in section 5.8.

6.4. Subject Screening and randomization Failures

Subjects that have signed the informed consent form but fail to comply with inclusion or exclusion criteria are considered screening failures. A screening failure 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 by mistake (e.g., if the investigator realizes that the subject is not eligible after the subject has been randomized), this is considered a randomization failure if the subject has not been treated and has no data registered on either the primary or the secondary endpoints. These subjects will not be part of the ITT population, but they will be part of the safety population.

6.5. 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 also 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.
- A subject will be considered lost to follow-up if at least three documented attempts (i.e., via certified letter) have been made to contact the subject and there is no response. If, after these attempts are made, and there is still no response, the subject will be withdrawn from the clinical investigation.

6.6. 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 designee, by a unique identification number (subject number) only.

Data entered on the eCRF are confidential and will only be available to the sponsor (including sponsor delegates), members of data management teams, the statistician, or Medical Advisor and if requested to regulatory authorities.

The principal investigator for each clinical investigation site will maintain as part of the investigator site file a list identifying all subjects entered in the clinical investigation (Subject Identification Code and Enrolment List). This list is confidential to all others than the Principal Investigator, or designee at the site.

7. Procedures

7.1. Clinical investigation-related procedures

Before initiation of the clinical investigation, Coloplast must be provided with key personnel's signed and dated curriculum vitaes (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 7.5: Schedule of Assessments for an overview of the clinical investigation-related procedures during subject visits, telephone visits, and at product/baseplate change.

7.2. Subject Visits

7.2.1. Screening Visit (Visit 0)

If a potential subject is interested in participating after the first contact, a visit (visit 0) will be arranged in a room reserved to ensure privacy and quiet surroundings at the investigator's clinic/department. When arranging the visit, it will be ensured, that the subject has received the Subject Information Form prior to the visit. 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 Visit 0 and to any possible 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.

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 give a urine sample for a pregnancy test. The sample will be destroyed right after the 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 that are deemed eligible per the inclusion/exclusion criteria are entered in the electronic data capture system and will be randomised to either treatment arm A or B.

Visit 0 and visit 1 can be combined.

7.2.2. Study visits (V1, V2 and V3)

During visit 1, baseline questions will be completed by the Principal Investigator, or designee. The subjects will be introduced to the clinical trial app and how to complete the questionnaires and take photos.

At test visit 1 and 2 investigational products (CE marked comparator products or non-CE marked Investigational Product) will be handed out according to the randomisation. The subject will only be informed about which product to wear in the upcoming period. At the visits, the subjects will be trained according to the IFU, in preparation of the product (e.g., hole size), preparation of skin before application (e.g., cleaning and wiping), application of the product (e.g., correct position and applying pressure to the baseplate), removal of product and storage of the product.

At each test visit the Principal Investigator, or designee, will ask the subject about any issues or concerns the subject may have had since last visit/call. The subject will, at each test visit, complete questionnaires about handling, preference, and quality of life. It must be ensured that the subject is provided a quiet room reserved to ensure privacy and is not disturbed when completing the questionnaires at the visit.

7.2.3. Telephone Calls

A follow-up call will be scheduled 7 days$^{-2/+2}$ after each test visit to ensure compliance with the clinical trial app and the provided product. Time between all other follow-up calls is 14$^{-3/+3}$ days, however the time between the

follow-up calls may not interfere with the test visit window. Additional calls may be scheduled if needed (assessed by the Principal Investigator, or designee).

During the subject phone calls (i.e., weeks 1, 3, 6, and 8 after visit 1), the Principal Investigator, or designee, calls the subject to follow-up since the last visit/call to ask whether the subject has had any problems or concerns.

7.3. Product change

Every time the subject changes a baseplate they will use the clinical trial app to complete a questionnaire about skin condition, reason for change, and use of accessories. In addition, they will be asked to take photos of the peristomal skin and the backside of the removed product.

7.4. 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 3). 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.

7.5. Schedule of Assessments

Assessment	Screening visit (V0)	Visit 1 (V1)	Every baseplate change	Visit 2 (V2)	Visit 3 (V3)	Telephone call (Weeks 1, 3, 6, and 8)
Informed consent	X					
Inclusion and exclusion criteria	X					
Pregnancy test (urine dipstick)	X					
Randomisation	X					
Subjects trained in skin preparation, Clinical Trial App, and Investigational product use according to IFU.	X	X		X		
Assessment of subject's wellbeing and compliance with CIP	X	X		X	X	X
Subject to take photos and complete questions in App			X			
Subject to complete QoL		X		X	X	
Complete eCRFs		X		X	X	
Dispense Investigational product according to randomisation		X		X		
Subject remuneration (if applicable)		X		X	X	

[redacted]

Assessment	Screening visit (V0)	Visit 1 (V1)	Every baseplate change	Visit 2 (V2)	Visit 3 (V3)	Telephone call (Weeks 1, 3, 6, and 8)
Confirm future visit and follow-up calls with subject	X	X		X		
Deviations	X	X		X	X	
Adverse Events		X		X	X	X
Device Deficiencies		X		X	X	X
Concomitant Medications	X	X		X	X	X

Table 1: Schedule of Assessments

7.6. Concomitant Medications

Concomitant medications will be registered in the eCRF. All concomitant medications the subject has taken from the time of consent through study termination will be collected.

7.7. Prohibitive Medications/Treatments

The skin undergoes major changes during radio- and or chemotherapy, and the skin might get more fragile to product changes. Therefore, subjects are not allowed to receive radio- and/or chemotherapy during the investigation. Low doses of chemotherapy or radiotherapy are allowed for indications other than cancer treatment (i.e., palliative care).

Steroid products on peristomal skin may interfere with the skin condition and make the skin more fragile to product changes. Therefore, subjects are not allowed to use topical steroid treatment on the peristomal skin area. Other systemic steroid treatment (e.g., injection or tablet) are not allowed. Low dose systemic steroid treatment (e.g., steroids used for asthma) are permissible if deemed appropriate by the investigator.

Subjects are not allowed to use barrier products during the investigation.

7.8. Supplementary materials and equipment

In addition to the investigational products, subjects will also be supplied with an iPhone and charger. They will be provided with toiletry bags to include items, such as scissors and disposal bags.

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, and laboratory testing.

Remaining risks needing further studies in humans can be described as follows:

A number of risks connected to use of the test product have been identified in the Product Risk Assessment. All risks will be mitigated before release of products for the clinical investigation. 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.

The following risks will be mitigated by actions during the clinical investigation.

- **Irritated skin (intact or non-intact):** Incorrect use of the product can lead to intact or non-intact irritated skin.

- **Tissue necrosis around the stoma:** Products with too small hole due to incorrect custom-cut, could lead to a squeezed stoma and therefore tissue necrosis around stoma.

To mitigate and reduce the risks, the subjects will be trained, according to the IFU, in preparation of the product (e.g., hole size), preparation of skin before application (e.g., cleaning and wiping), application of product (e.g., correct position and applying pressure to the baseplate), removal of product and storage of the product.

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

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

8.2. Risk-benefit analysis for the conduct of the clinical investigation

The test products contain a protecting layer that should help protect the skin from leakage induced skin damage, which could be beneficial for the subjects. The outcome of this investigation will contribute with important information for development of products for subjects with a stoma, regarding protecting the skin from leakage induced skin damage.

Disadvantages during the investigation could be the extra workload related to completion of questionnaires, visits at site and using the clinical trial app at each change of product. The subjects may be asked to use a [redacted] that is not their usual size.

The participating subjects will contribute with important information for development of new stoma products, that may reduce peristomal skin complications. Due to the actions taken to mitigate the above-mentioned 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, but they may benefit from the use of the new stoma product through less irritated peristomal skin and improved quality of life in the future.

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. A risk-based monitoring strategy may be used including on-site, remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

8.3. Delegation of responsibility

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 Principal Investigators and designees will receive training in all aspects of the investigation and before they can begin any investigational related tasks. The training must be documented in the 'Clinical Investigation Training Log' at each site. The Principal Investigator is responsible for maintaining these logs.

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).

In some cases, the monitoring of this clinical investigation has been delegated by the sponsor to CRO. 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 the purpose of 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 requirement(s).

The monitoring process is briefly described below and is described in more detail in the Monitoring Plan.

The monitoring will be conducted periodically at all sites 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

9.1.1. Site Selection visit

Depending on the prospective clinical investigation site's 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. Site Initiation visit

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

All clinical investigation sites will get an initiation visit during which full training on all aspects of the clinical investigation will be provided. This visit can be done on-site or remotely.

9.1.3. Site Monitoring visit(s)

The site dedicated monitor is to ensure adherence to the clinical investigation plan, accurate data recording on the eCRFs 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 personnel, however the role and time period of involvement for each clinical site personnel must be documented on the delegation log. Training for all delegated site personnel will be documented on the training log before any involvement with the clinical investigation.

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.

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 and the Subject's Clinical Trial App, will be performed by Coloplast CM throughout the conduct of the investigation. See section 9.3.

9.2. Source data verification

A source document is a document in which data collected for a clinical investigation is first recorded. This data is usually later entered in the 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 clinical investigation.

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 ensure 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. In some cases, 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.

Only the Principal Investigator, or designee, and the sponsor representatives will have access to all the eCRFs. The subject will have access to questionnaires and diaries completed in the Clinical Trial App.

9.3. Remote monitoring

Remote or centralized monitoring is a remote evaluation carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than the site(s) at which the clinical 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 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 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 eCRFs 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.

10. Statistical considerations

10.1. Statistical design, method, and analytical procedures

The primary objective will be evaluated by analysing the primary endpoint. The analyses of the exploratory endpoints [redacted] will be used to further evaluate and explore the primary objective. The secondary objective will be evaluated by analysing the secondary endpoint (the DLQI score) and further explored by analysing the DLQI sub-scale.

All baseline measurements, endpoints and assessments will be summarized by descriptive statistics and/or listed. Endpoints and assessments will be summarized by product and product type (1-piece or 2-piece). 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.

The pass criteria for the study is based on the result from the analysis of the primary endpoint and therefore no adjustment for multiple testing will be applied.

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

10.1.1. Definition of analysis populations

Intention to Treat (ITT), Safety and Per Protocol (PP) 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 randomised subjects with valid informed consent who have been exposed to at least one product, with information on at least one product with respect to either primary or secondary endpoints.

The PP population will constitute a subset of ITT subjects:

- who fulfill the inclusion/exclusion criteria
- where the primary endpoint, the decision tree score, is present in at least one of the steady state periods

- who have not used another product other than the randomized product for more than 3 days in a row at steady state
- who do not have a major deviation, as defined in section 13.0. Any exclusion of subjects from the PP/ITT population must be documented. Invalid individual data points may be omitted from analysis even though the corresponding subject is part of the ITT or PP population. Any exclusion of data points will be documented.

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

All statistical analysis will be based upon the ITT and PP 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/PP population.

10.1.2. Analysis of the primary endpoint

Decision Tree (DT) score measured at each baseplate change at steady state will be analysed by a mixed repeated measures model using individual baseplate scores (on a scale from 0-3) as the observational unit. 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 (comparator product, test product), a fixed effect of product type (1- or 2-piece), a fixed interaction between product and product type, a fixed period effect, an interaction between period and product describing a possible carry-over effect, a random effect of subject, a random interaction effect of product and subject and a random residual error.

All combinations of differences between the two products will be estimated for both 1- and 2- piece products. Furthermore, differences for same product between product types will be estimated. If the interaction between product and product type is non-significant, the difference between the two products will be estimated.

As a sensitivity analysis, the primary analysis will be repeated including only subjects that have observations in both treatment periods. Hence the imputation of possible missing values can be evaluated.

10.1.3. Analysis of the secondary endpoints

The total Quality of Life (DLQI) score from Visit 2 and 3 will be analysed by a linear mixed model similar to the model for the primary endpoint, except that the random interaction effect of product and subject is not included, as there is only one measurement per subject for each product.

10.1.4. Analysis of exploratory endpoints

[redacted]

[redacted]

10.1.5. Analyses of safety endpoints

Adverse events will be listed and summarized, if relevant. Device deficiencies and concomitant medication will be listed.

10.2. Sample size

The Decision Tree (DT) score will be calculated at each baseplate change. A Severe score is equal to 3 whereas Moderate is 2, Mild is 1 and Not treatment required is 0. It is assumed that data are distributed in all 4 categories and therefore can be analysed by a model assuming normally distributed data.

The sample size calculation is based on a simplified linear mixed model with no effect of product type and no period effect. The model includes a fixed effect of product (comparator and test product), a random effect of subject and a random interaction effect of product and subject. As the sample size does not distinguish between product type it is assumed that both 1- and 2-piece users uses approximately 10 baseplates in the steady state period. This means, the power of the analysis might be in favour of 1-piece users if the final model is not combined as 1-piece users might use more products.

Based on data (PP population) from the previous CP288 investigation, it is assumed that the total standard deviation of the primary endpoint is 1.1 and that the total variation 1.1^2 is divided so that:

- a random effect of subject accounts for 46% of the total variation
- a random interaction effect of product and subject accounts for 9%
- and the residual accounts for 45% of the total variation

In the below table the needed sample size is calculated by simulation for varying values of the true difference between comparator and test product regarding mean DT score and for different values of the power to demonstrate that the difference is significantly different from 0.

Table 2: Subjects needed for comparing mean DT score (scale 0-3) between two products

True Difference	Reduction in mean if the mean for the comparator is 2.0 as for [redacted] in CP288	Power			
		0.8	0.85	0.9	0.95
0.2	10%	64	>70	>70	>70
0.3	15%	30	35	40	50
0.4	20%	<20	20	24	30
0.5	25%	<20	<20	<20	20

Based on interpolation between the numbers in the table, 33 subjects should test each product to ensure a power of 96%, if the true difference between the comparator product and a test product is 0.4 (clinically relevant difference according to the validation of the DT score). Correspondingly, 33 subjects will ensure a power of 83% if the true difference is 0.3 (still within the 95% confidence interval for the clinically relevant difference according to the validation of the DT score). 1-piece and 2-piece users will be evaluated separately (in a

combined model). Hence 33, 1-piece and 33, 2-piece users will be needed to complete the study. In case there are no significant difference between type of product the 66 users will be analysed in a reduced model. If the true difference is only 0.2 then 66 subjects should ensure a power of 82% to detect the difference as significantly different from zero but still within the 95% confidence interval for the clinically relevant difference. To take a potential drop-out (20%) into account it is recommended to include a total of 41 1-piece and 41 2-piece users, resulting in a total of 82 subjects.

If the recruitment target of 82 subjects is not reached within the timelines, the recommendation is to prolong the timelines to reach the recruitment target. This is to avoid a situation of not showing a significant result due to the power being too low.

10.3. Level of significance and power

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

10.4. Pass/fail criteria

The purpose of the investigation is fulfilled if a statistically significant improved difference in the primary endpoint is obtained with the test product compared to [redacted]

11. Data management

11.1. Data collection and data management

11.1.1. Data Collection in the clinical investigation

Data management and statistical analyses are carried out by [redacted] Coloplast A/S.

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

The EDC system used is [redacted], delivered by [redacted] ystem 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 Principal Investigator, or designee, 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 Principal Investigator, or designee, 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 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.

The DLQI questionnaire will be completed by the subject and entered into the eCRF by site personnel.

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

The subject will receive an iPhone with the Clinical Trial App installed. The app is developed on behalf of Coloplast A/S by the app development company Nodes. This Clinical Trial App is used during the investigation every time the subject makes a product (1-piece) or baseplate (2-piece) change.

The photos and the data completed in the Clinical Trial App are transferred via an encrypted connection to a Coloplast controlled [redacted] environment. Photos will be stored and can be assessed at [redacted]. All other data will be transferred automatically into the EDC system.

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

In the unforeseen situation, where site cannot establish connection to the EDC system a paper CRF (pCRF) has been printed and supplied by sponsor.

The Principal Investigator will keep a separate list of the subjects' ID numbers, enrolment date, randomisation number, date of birth, names, phone number, email and addresses in a locked room/cabinet. Only data referred to in this clinical investigation plan will be recorded in the CRFs.

11.1.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The Principal Investigator, or designee 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 designee, 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, or designee, 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. 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 EC and applicable regulatory authority. Substantial changes may require approval from the EC and applicable regulatory authority prior to implementation.

13. Deviations from the Clinical Investigation Plan

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

A minor deviation is defined as those that do not increase risk or decrease benefit or do not 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 well-being 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 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 periodic monitoring report and any actions for additional follow up are addressed with the Investigator.

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.

Details about the deviation will be collected, for example:

- Site ID
- Subject ID
- Deviation Date
- Clear and concise description of the event
- The reason for the deviation and any corrective action taken, including the date of the corrective action.

If applicable, record the EC notification date and retrieve a copy of the EC Submission Letter for the eTMF.

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 investigational devices to the investigational sites until return of or disposal.

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

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

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.
- 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 clinical investigation plan 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 personal information provided by the subject for the investigation ("subject personal data"). This includes identification and contact information, which will be pseudonymized. Prior to visit 1, the subject will be randomised to either treatment Arm A or B and will be allocated a randomisation number. as well as information about the subject's product usage experience and 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 Principal Investigator, or designee). Such cases will imply a transfer of personal data to the third parties, but solely for the specified purposes and with the third

[redacted]

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.

15.4. Financial conditions

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

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 designee. 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 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

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.

17.2. Compensation for participating in the clinical investigation

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

Subject payment/subject/visit	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

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, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

Temporary redness upon removal of the baseplate is not considered to be an adverse device effect. However, an abnormal development in the intensity or duration of redness should be considered an adverse device effect. A development in redness after removal of the baseplate is considered abnormal, when the intensity of redness is not decreased after five-ten minutes after the baseplate has been removed.

18.3. Device deficiency

A device deficiency is the inadequacy of the investigational 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.

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.

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

All adverse events and device deficiencies will be reported in the eDC, [redacted] database. If, for some reason, the system is off-line, investigators (or designee) are required to report the event to: [redacted]

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 where 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.

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.

18.8. Sponsors Reporting Responsibilities

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

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

18.9. 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.

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

The clinical investigation report must be submitted to EC and regulatory authorities.

21. Publication policy

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 (if sub studies are performed using an umbrella CIP, results and conclusions for each sub investigation can 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. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if:

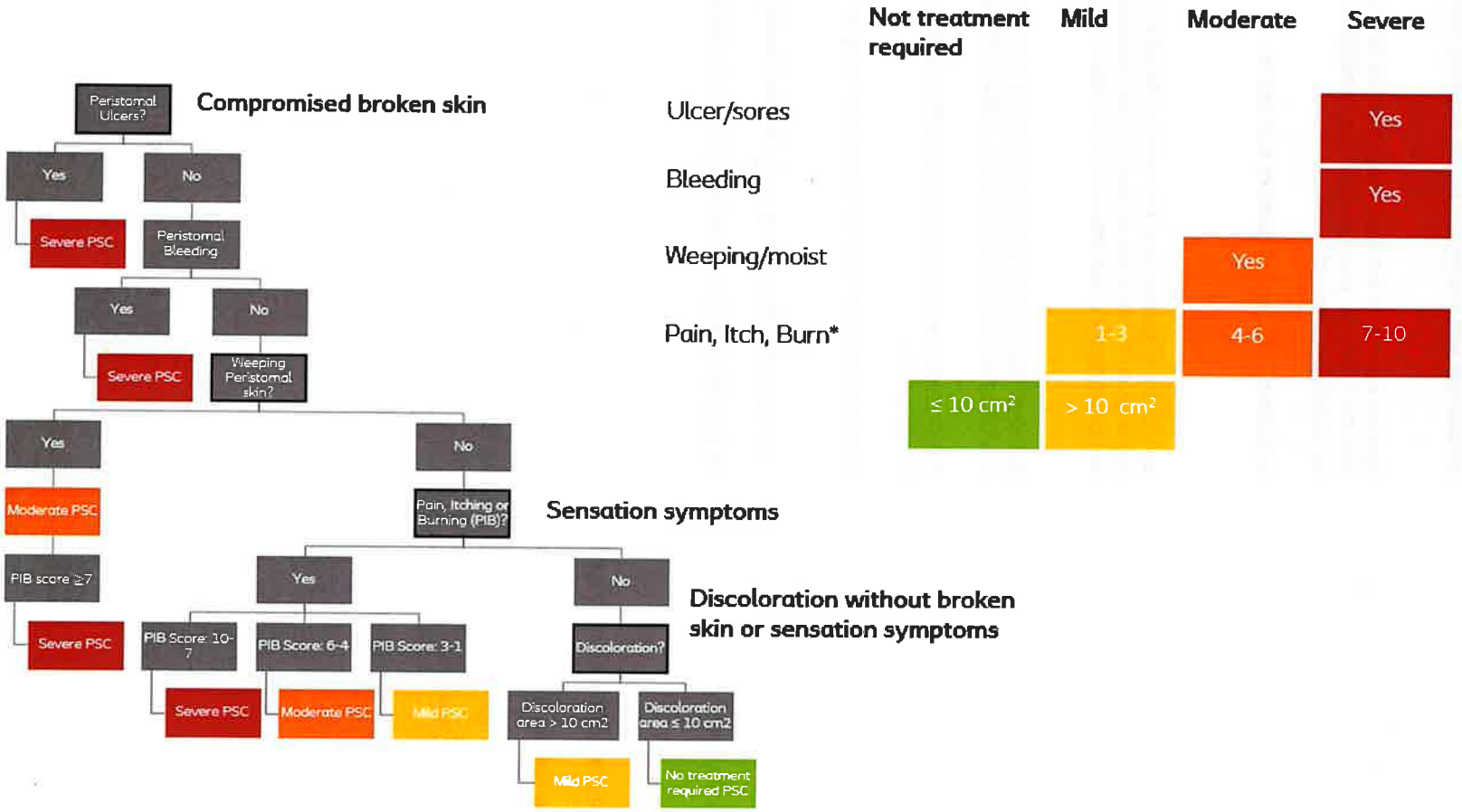
- major non-adherence to the clinical investigation plan is occurring
- it is anticipated that the subject recruitment will not be adequate to meet the investigation objectives [at least 75%] of the subjects should be entered within the recruitment time.

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

23. Appendices

Appendix 1: Ostomy Skin Tool V2.0 - Decision Tree Score

The PRO data from OST V2.0 and the image analysis data are combined in a Decision Tree model to provide an overall skin complications severity level for each patient. The Decision Tree model provides a hierarchy of scores and assigns patients a skin severity level based on the observed combination of these variables, as outlined below.



*Pain, itching, and burning severity items on a scale from 0-10 mapped together constitutes the PIB score, which is the highest value of pain, itching and burning

[redacted]

Appendix 2: Dermatology Life Quality Index Questionnaire

(https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index)

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

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[redacted]

Appendix 3: CP338 Endpoints and Assessments

	Endpoints and assessment	Assessed by	V1	V2	V3	Follow-up calls (Call 1-4)	Baseplate/ Product change
Primary endpoint	**Decision Tree Score on baseplate level at steady state (scale from 0-3)** **Skin condition** Ostomy Skin Tool V2.0 (Appendix 1 and 4)	**Sponsor, based on subject reported outcomes via Ostomy Skin Tool and discoloration area**					X
Secondary endpoint	**Health-related quality of Life (DLQI) score evaluated at the end of each test period (scale from 0-30)** (DLQI questionnaire, Appendix 2)	**Subject**	X	X	X		
[redacted]	[redacted]	[redacted]					X
	[redacted]	[redacted]					X
	[redacted]	[redacted]					X
	[redacted]	[redacted]					X
	[redacted]	[redacted]					X
	[redacted]	[redacted]					X
	[redacted]	[redacted]	X	X	X		
	[redacted]	[redacted]			X		

[redacted]

	[redacted]	[redacted]			X		
Safety endpoints	Adverse Event	Investigator	X	X	X	X	
	Device deficiencies	Investigator	X	X	X	X	
	Concomitant medication	Investigator	X	X	X	X	

[redacted]

Appendix 4: Ostomy Skin Tool V2.0 – PRO (Patient Reported Outcome) Questionnaire

The OST V2.0 comprises a PRO questionnaire consisting of six items designed to assess the severity of peristomal skin complications.

Patient questionnaire

Patient number: _____ ___ **Date:** __/__/____

Instructions

These questions should be completed by the patient themselves. The following questions ask about the skin complications you experience around your stoma (from the stoma site to the edge of the stoma bag adhesive). Please answer each question thinking about right now when changing your product.

Question 1. Do you experience any **bleeding from the skin** around your stoma **right now** when changing your product? (tick one box only)

☐ Experiencing	☐ Not experiencing

Question 2. Once you have cleaned and dried the skin, do you still experience any **weeping or moisture on the skin** around your stoma **right now when changing** your product? (tick one box only)

☐ Experiencing	☐ Not experiencing

Question 3. Are you experiencing any **ulcers or sores** around your stoma **right now** when changing your product? (tick one box only)

☐ Experiencing	☐ Not experiencing

Instructions

The following questions ask about the skin complications you experience around your stoma (from the stoma site to the edge of the stoma bag adhesive). Please answer each question thinking about the period since you last changed your product until now.

Question 4. Please rate on a scale from 0-10 how itchy the skin around your stoma has been at its worst since you last changed your product (tick one box only)

☐ 0 No itch	☐ 1 Very mild itch	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10 Worst possible peristomal skin itch

Patient questionnaire

Patient number: _____ ___ **Date:** __/__/____

Question 5. Please rate on a scale from 0-10 how **painful** the skin around your stoma has been at its worst since you last changed your product (tick one box only)

☐ 0 No pain	☐ 1 Very mild pain	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10 Worst possible peristomal skin pain

Question 6. Please rate on a scale from 0-10 any burning feelings from the skin around your stoma at its worst since you last changed your product (tick one box only)

☐ 0 No burning	☐ 1 Very mild burning	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10 Worst possible peristomal skin burning

[redacted]

Appendix 5: Baseline Data Collected

The following baseline data will be collected and registered at the screening visit (V0) by the investigator or designee:

- Date of Informed Consent
- Subject number
- Date of visit
- Check of inclusion criteria
- Check of exclusion criteria
- Complete randomization

Demographic Data:

- Age at time of enrollment (years)
- Gender (male/female)
- Height (cm)
- Weight (kg)

Stoma Details:

- Age of stoma (month (if available) and year when created)
- Type of stoma (ileostomy/colostomy)
- Cause of the stoma (Crohn's disease/Colitis ulcerosa/ Cancer/ Other)
  - If "other", please explain (text).
- Size of the stoma (diameter on widest place and height)
- Shape of the stoma (round/oval/irregular)

Current product details:

- What is your current [redacted] details (lot number, item number, product type (1-piece/2-piece))?
- Are you used to cutting the baseplate? (Yes/No)
  - If yes, how much is cut off from the baseplate *(min and max cut in mm)*?
- Which stoma accessories do you normally use? *(You may tick more than one box)*
  - None
  - Adhesive remover
  - Paste
  - Rings
  - Stoma tape

[redacted]

- Stoma belt
- Hernia belt
- Stoma powder
- Barrier lotion/cream/spray/wipes
- Cleansing wipes/cleansing spray
- Odour remover
- Other accessories
  - If 'other accessories', please specify.

- On average, how often do you normally change your product (1-piece)/baseplate (2-piece)?
  - Once or more per day
  - Every second day
  - Every third day
  - Every fourth day
  - Every fifth day
  - Every sixth day
  - Once a week or less frequent

Peristomal skin complication details:

How often do you experience the following peristomal skin complications?
- Itching peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Burning peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Painful peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Bleeding peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Weeping/moist peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Broken/ulcered peristomal skin)? (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)
- Red/discoloured peristomal skin (Daily, Every 2-3 days, Every 4-6 days, Every 7 days, Once every second week, More rarely)

Fecal output details:

- What is the frequency of your fecal output? (All the time (continuous)/with regular intervals/with irregular intervals)
- Do you experience ballooning (air in the bag)? (Yes/no)
- What is the consistency of the output evaluated on the Bristol Scale? (Type 1-7)

Appendix 6: Only to be used for subjects with a colostomy. To be included people with a colostomy need to have liquid fecal output (type 6-7 on the Bristol 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

[redacted]

Appendix 7: Pictures of Different Types of Leakage

Text to go with the pictures: Below you see different pictures of baseplates which is shown from the back (the part sticking to your body). The brown colour indicates faeces coming in contact with the baseplate. All pictures within the turquoise frame are considered leakage.

Figure 1

Not considered leakage
The adhesive change colour and swells due to absorption of moisture
(Figure 1)

Figure 2

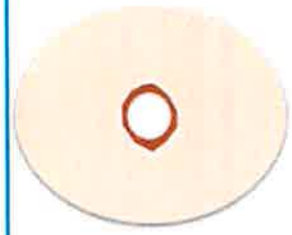

Figure 3

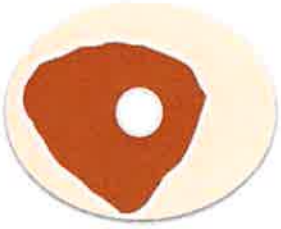

Figure 4

Figure 5

Considered Leakage
Output under the baseplate (with or without soiling the clothes)
(Figure 2, 3, 4 and 5)

[redacted]