Clinical Investigation Plan

CP275

A clinical investigation evaluating three new 1-piece ostomy products.

April 2017 – May 2018.

Master

CHANGE LOG

[redacted]

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> SYNOPSIS OF THE CLINICAL INVESTIGATION

Objective

The **aim** of the study is to investigate and understand how the peristomal skin react if 1) the topfilm on existing ostomy products is changed to a softer topfilm or 2) the adhesive is changed but the topfilm is the same.

Primary endpoint and secondary endpoint(s)

The primary objective is to investigate the impact change of a new topfilm or adhesive (on an existing ostomy product) has on mechanical trauma on the peristomal skin.

Secondary objectives are

- To investigate the impact change to a new topfilm or adhesive (on an existing) has on the handling (application and removal) of the product.
- To evaluate which combination of adhesive and topfilm that has less negative impact on the peristomal skin
- To evaluate which combination of adhesive and topfilm that is most easy to handle (application and removal)

Pass/fail criteria

No formal success criteria are applied in this explorative investigation. The investigation will provide valuable insight into how the peristomal skin react if the topfilm on existing ostomy products is changed to a softer topfilm or the adhesive is changed but the topfilm is the same on an existing product.

Design of the investigation

The investigation is an explorative, open-labelled, randomised, controlled, comparative study investigating three ostomy test products based on the CE-marked SenSura Mio (1-piece Open Flat) and SenSura (1-piece Open Flat). The study is designed with a run-in period and two test periods. The run-in period (14 days) is for potential subjects not currently using a SenSura Mio (1-piece Open Flat) or SenSura (1-piece Open Flat) product. The first test period includes use of 7 (+/-1) products (own) and the second period includes use of 14 test products (+/-1 product). As subjects needs to change minimum every second day, each subject will be enrolled for maximum 42 (+/-5) days. The subjects using SenSura Mio will be randomised into one of two possible treatment groups. Subjects using SenSura will not be randomised as only one treatment arm is available. (see figure 1). Each treatment arm consists of two test periods in which the subjects will test their own product followed by the test product. The subject will receive 1 box with 20 test products. During the investigation, there will be 6 visits, where visit 0 will be the information visit.

Population

The investigational population consists of Danish colostomy/ileostomy-operated subjects that comply with the following inclusion criteria:

1. Have given written informed consent and in DK: signed a letter of authority
2. Be at least 18 years of age and have full legal capacity
3. Have had their colostomy/ileostomy for at least three months
4. Have a colostomy/ileostomy with a diameter between 10 and 55 mm
5. Be able to handle the Clinical App. and product themselves
6. Must be able to use custom cut product
7. Minimum change of product every second day
8. If current product is SenSura Mio - Be willing to use Maxi bag during investigation
9. Subject using SenSura or SenSura Mio flat 1 pc. open for at least two weeks before inclusion in the study.
10. Negative result of a pregnancy test for women of childbearing age (only DK)

And exclusion criteria:

1. Are currently receiving or have within the past 2 months received radio-and/or chemotherapy (low doses chemotherapy are allowed for other indications than cancer, e.g. below 15 mg methotrexate for rheumatoid arthritis)
2. Are currently receiving or have within the past month received topical steroid treatment in the peristomal skin area, e.g. lotion or spray. Systemic steroid treatment (e.g. injection, or tablet) are allowed.
3. Are pregnant or breastfeeding**
4. Are participating in other interventional clinical investigations or have previously participated in this investigation
   - Exception: Participation in other Coloplast in-house clinical investigations are accepted under the circumstances that the subject has paused the activities in the investigation and are otherwise complying with the inclusion and exclusion criteria of this protocol (CP275)
5. Are currently suffering from peristomal skin problems i.e. bleeding and/or broken skin (assessed by the investigator)
6. Have known hypersensitivity towards any of the products used in the investigation

Test products

The test products are non-CE-marked, non-sterile, class 1, Coloplast 1-piece open ostomy appliances with hide-away bag which is intended for use in collecting output from ileostomies.

Investigation approval

The investigation will be approved by the EC in Denmark and the Danish and Medicines Agency before investigation initiation.

> LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 15.1
AE	Adverse Event	See section 15.1
ASADE	Anticipated Serious Adverse Device Effect	See section 14.3.3
CIP	Clinical Investigation Plan	
CRF	Case Report Form	Questionnaire to be used for data collection
CTM	Clinical Trial Manager	
DQF	Data Query Forms	A DQF is a query specifically used in clinical research. The DQF is the primary data query tool from the sponsor to clarify discrepancies and ask the investigator for clarification. The DQF is part of the data validation process in a clinical investigation.
EC	Ethics Committee	
IB	Investigator's Brochure	Compilation of the current clinical and non-clinical information on the investigational medical device(s,) relevant to the clinical investigation.
IFU	Instruction For Use	
ITT	Intention to Treat	
PI	Principal Investigator	Qualified person responsible for conducting the clinical investigation at an investigation site. If the clinical investigation is conducted by a team of individuals at an investigation site, the PI is the responsible leader of the team. Whether this is the responsibility of an individual or an institution can depend on national regulations.
PP	Per Protocol	
SADE	Serious Adverse Device Effect	See section 15.3
SAE	Serious Adverse Event	See section 15.3
USADE	Unanticipated Serious Adverse Device Effect	See section 15.3

> SIGNATURE PAGE

All Sponsor parties declare by their signature on the electronic signature page to follow the Clinical Investigation Plan CP275 in accordance with the Declaration of Helsinki, ISO 14155 and the Medical Device Directive.

SPONSOR

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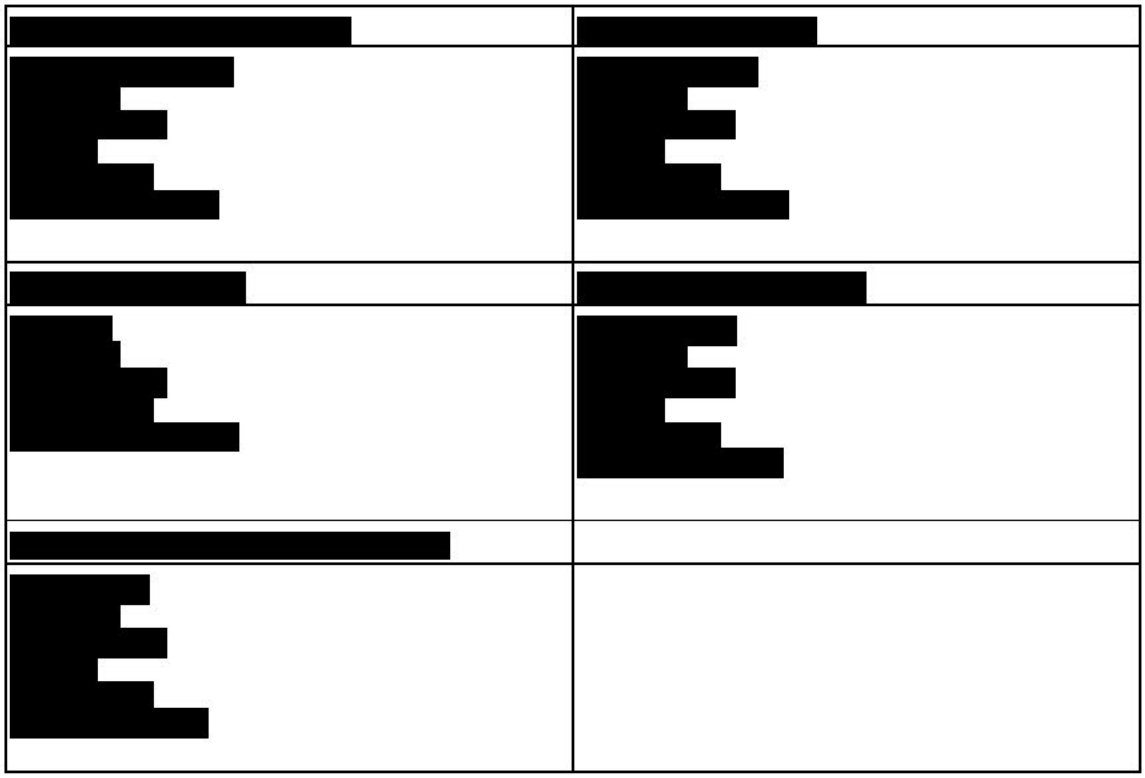
2. List of personnel involved in the Investigation

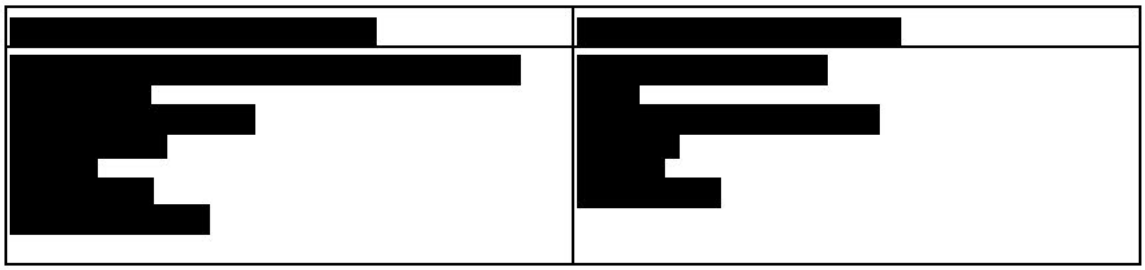
2.1. Sponsor representatives



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

2.2. Investigators

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



2.3. Other

External study nurses will be in-sourced to help conducting the site visits together with Coloplast personnel.

3. Identification and description of the investigational device

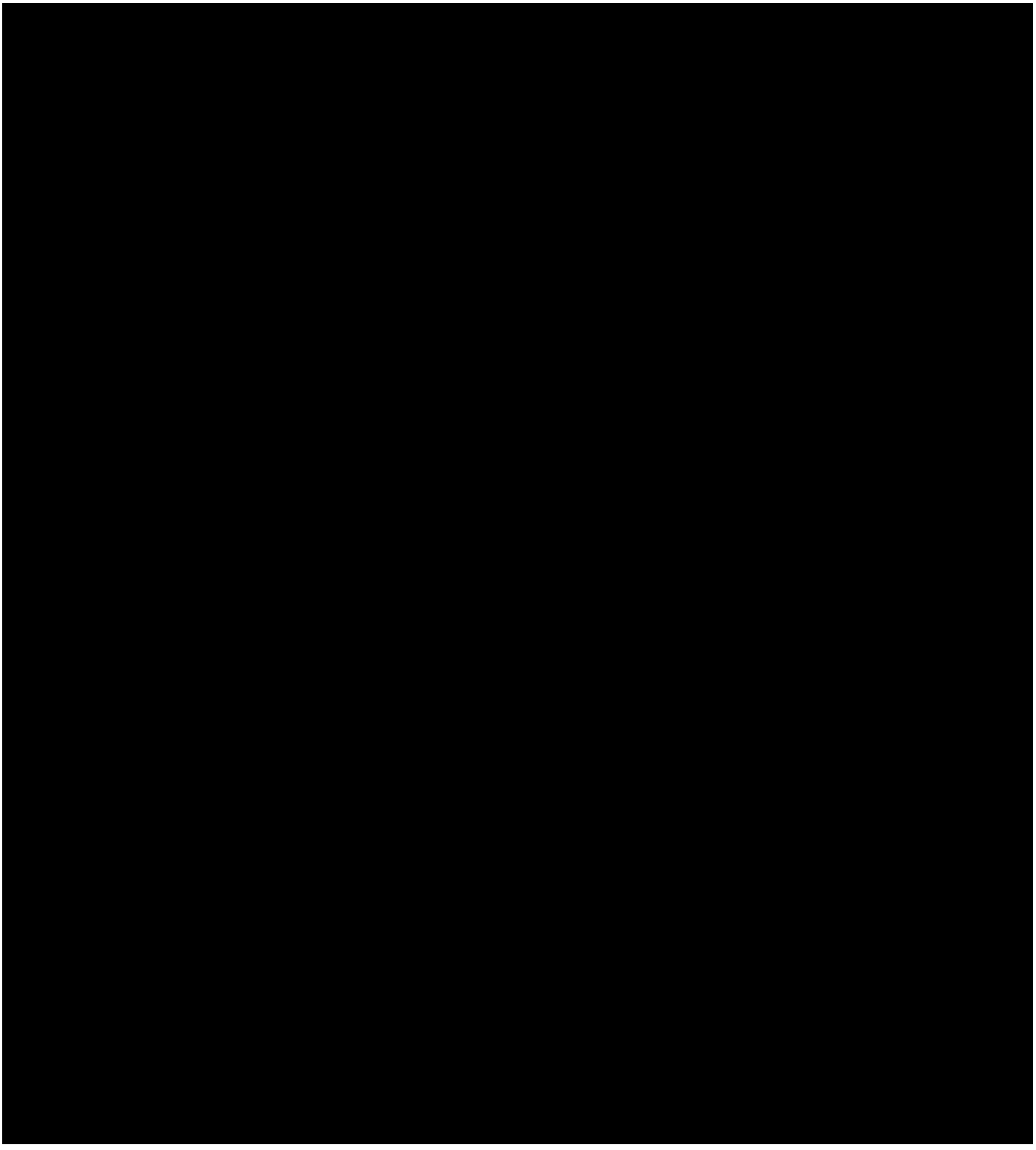
The test products (ostomy appliance) which are tested in the CP275 clinical study are developed for people with an ileostomy requiring a flat 1-piece solution.

3.1. Manufacture

Coloplast A/S, Holtedam 1, 3050 Humlebæk, Denmark, manufactures the investigational device.

3.1.1. Identification, traceability and labelling of device

The test products (ostomy appliance) will be packed in retail boxes with 20 devices in each box. Each retail box will be provided with a production lot number. The examples below for test products 1A and 1B show a label that will be attached to each box in order to secure traceability and identification of the test products. Each label will contain the description of the actual product. Labels for test products 2A, 2B, 3A and 3B will have a similar label attached. See Investigators brochure. [5].



3.1.2. Clinical investigation purpose of device

The test product is designed to collect output from a stoma. The adhesive is intended to adhere to intact peri-stomal skin.

3.1.3. Intended population for the device

The intended population for the test products are subjects with a stoma. The intended population in the present investigation are subjects with ileostomy currently using a 1-piece flat product. For more details and justification for choice of the population in the present investigation, please see section 7.3

3.1.4. Description of investigational device

The test products are non-CE-marked, non-sterile, class 1, Coloplast 1-piece open ostomy appliances with hide-away bag which is intended for use in collecting output from ileostomies.

[redacted]

Only open bags are available in the investigation. If a subject is used to a closed bag (e.g. if having a colostomy), then he/she will be instructed to use the open bags as closed bags – e.g. not opening the outlet, but changing the product just as often as he/she would normally do. Subjects, who normally use a closed bag, are instructed to and shown how to use the open bag as a closed bag by the investigator or trained study personnel.

Test Product 1 & 2 are 1 piece (1p) open ostomy bags are designed for people with an ileostomy (Figure 1, based on the SenSura Mio Bag). [redacted]

[redacted]

The adhesive wafer consists of two adhesives coated onto a top film. The skin side of the adhesive wafer is covered by a release liner on which a cutting guide is printed, allowing the user to cut/choose a suitable size hole for his/her stoma.

Test product 1:

[redacted]

Test product 2:

[redacted]

[redacted]

Figure 1: Test Product 1 & 2 1p. open bag.

Test Product 3 - 1-piece (1p) open ostomy bags are designed for people with an ileostomy. [redacted]

Test product 3:

[redacted]

[redacted]

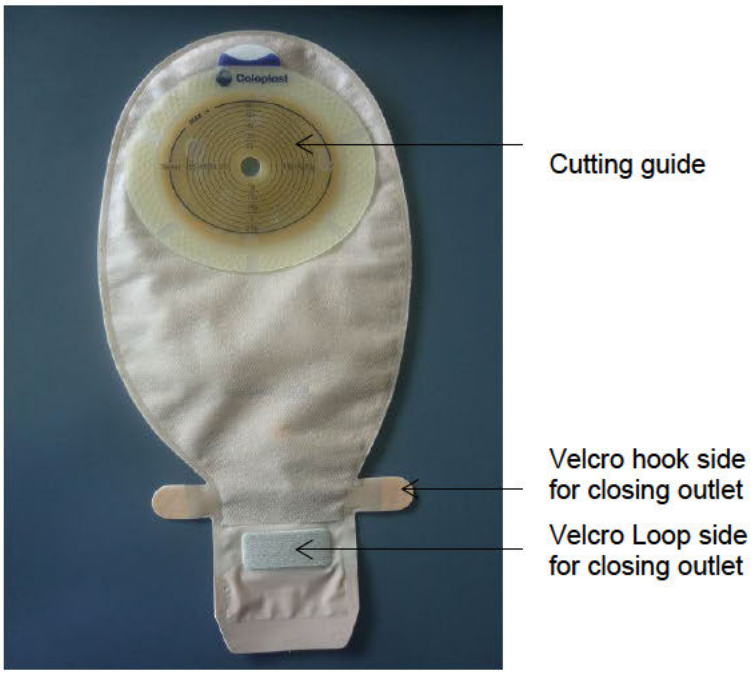


Figure 2: Test Product 3 1-piece open ostomy bag, viewed from the side facing the skin. [redacted]

3.1.5. Handling and training

The handling of the test products is described in details in the IFUs, which is included in all boxes with test products. The test products must be stored horizontally under cool and dry conditions, away from direct sunlight and are for single use. Reprocessing, washing, disinfection, and sterilization may compromise product characteristics, causing additional risk of physical harm to or infection of the user. Each subject will be instructed by investigator/investigator representative in how to handle the test products according to the IFUs. [5].

3.1.6. Comparator product(s)

SenSura Mio (1-pc flat open) or SenSura (1-pc flat open) will be used as comparators. As the comparator products are already on the market and will be used within the intended use in this clinical investigation, it is not considered an investigational device according to ISO 14155:2011 and is thus not described here. Please refer to the ISO 14155:2011 for details.

4. Justification for the conduct of the clinical investigation

People with abdominal stomas have, despite development of better ostomy products, still problems with leakage and peristomal skin disorders which influence their quality of life negatively. [1,2].

In this study we want to seek knowledge on how ostomy users handle their products and deals with the challenges of using an ostomy appliance. [redacted]

[redacted]

5. Investigational device and clinical investigation risks and benefits

The clinical investigation is conducted in accordance with current law and applicable standards see section 13. The rights, safety and well-being of human subjects shall prevail over interest of science and society. All study personal and the investigator and investigator representatives will all be instructed in performing their job with conscientiousness and care.

5.1. Anticipated benefits

[redacted]

5.2. Anticipated risk, side effects and disadvantages

No other risks are expected than the anticipated adverse events described in Section 15.1, all of which are well known in connection with the use of ostomy devices. The risk assessments of the test products will be

conducted in accordance with ISO 14971 requirements. There is no known interaction between the use of ostomy devices and concomitant medication.

5.3. Benefits versus risks

[redacted]

6. Objectives and hypotheses of the clinical investigation

6.1. Objective

The primary objective is to investigate the impact change of a new topfilm or adhesive (on an existing ostomy product) has on mechanical trauma on the peristomal skin.

[redacted]

6.2. Claims and intended performance to be verified

[redacted]

6.3. Risks and anticipated adverse device effects to be assessed

The anticipated adverse device effects are well known in connection with the use of a new ostomy product. Allergic peristomal skin irritation occurs very rare, but information about possible allergic reactions will be collected.

Temporary redness upon removal of the base plate 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.

There is no known interaction between the use of ostomy devices and concomitant medication.

7. Design of the clinical investigation

Overall study characteristic:

- Run-in period of potential participants using other products than the defined comparator products and who are willing to use either SenSura Mio (1pc open flat) or SenSura (1pc open flat) for a screening period of 14 days to accommodate the inclusion criteria of the study.
- Open-labeled
- Controlled
- Randomisation between subjects using SenSura Mio to either test product 1 or test product 2
- Comparison to either SenSura or SenSura Mio (1pc open)
- Colo- and ileostomy subjects

Figure 2: Investigation with three products. There is a total of three combination possibilities.

7.1. General

The investigation is an explorative, open-labelled, randomised, controlled, comparative study investigating three ostomy test products . The study is designed with a run-in period and two test periods. he subjects will be asked to use one of the above mentioned CE-marked products for 14 days to get used to the product before a potential inclusion to the investigation. The product used in the run-in period will be considered as the subjects own product. Subjects who have SenSura Mio (1-piece Open Flat) or SenSura (1-piece Open Flat) as their current product (own product) can participate in the investigation without the run-in period.

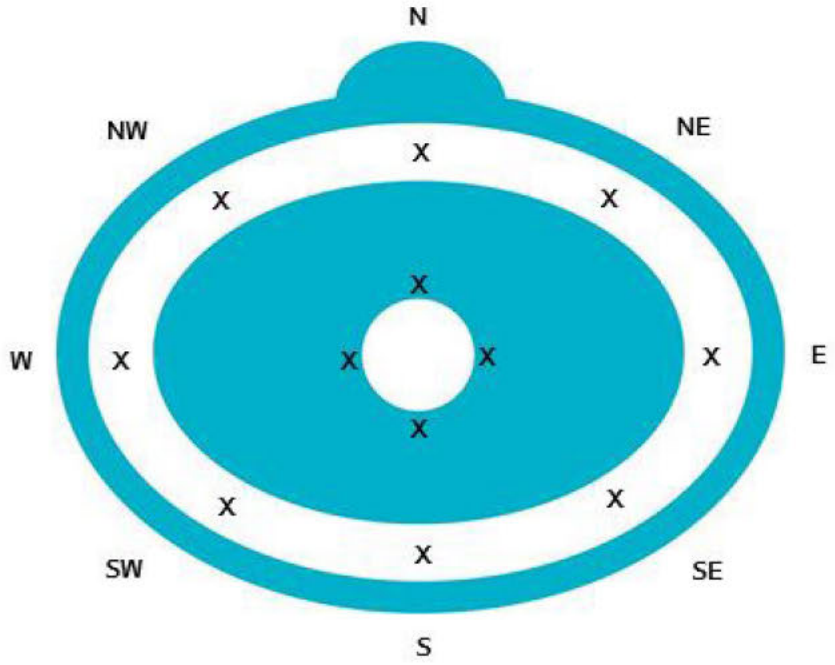
The first test period includes use of 7 (+/-1) products (own) and the second period includes use of 14 test products (+/-1 product). As subjects needs to change minimum every second day, each subject will be enrolled for maximum 42 (+/-5) days.

The subjects using SenSura Mio will be randomised into one of two possible treatment groups. Subjects using SenSura will not be randomised as only one treatment arm is available. Each treatment arm consists of two test periods in which the subjects will test their own product followed by the test product. The subject will receive 1 box with 20 test products. During the investigation, there will be 6 visits, where visit 0 will be the information visit.

7.1.1. Primary endpoint

Primary endpoint:

Trans Epidermal Water Loss (TEWL) measured at 8 places (N, NE, E, SE, S, SW, W and NW) of the outer edge of the baseplate.



[redacted]

Baseline data

a) Gender
b) Age
c) Weight
d) Height
e) Type of stoma (ileostomy/colostomy)
f) Duration of colostomy/ileostomy (year when created)
g) Cause of the stoma (Crohn's disease/Colitis ulcerosa/Cancer/Other)
h) Size of the stoma (diameter on widest place and height)
i) Body check profile questionnaire (box 4: non or superficial creases/ Deep folds)
j) Current product (brand, product name, item number, size)
k) Use of accessories
l) How often is the ostomy appliance normally changed? (At least twice a day/Once a day/Every 2nd day/Every 3rd day or more rare
m) Randomized testproduct
n) Run-in period (yes/no)

After each product change during each test period:

Handling of base plate (application, removal)

a) How did you find detaching the base plate you just removed? (very difficult/ difficult/ acceptable/easy/very easy)
b) How did you find attaching the base plate you just applied? (very difficult/ difficult/ acceptable/easy/very easy)

Body fit/freedom of movements

a) How was the base plate's ability to fit to the body contours in the area around the stoma? (very poor/poor/acceptable/good/very good)

b) How was the base plate's ability to bend and stretch with your skin when your body moves? (very poor/ poor/ acceptable/ good/very good)

What was the **main** reason for changing the product?

☐[1] I followed my usual changing pattern

☐[1] I thought it would be nice with a clean product

☐[1] In preparation of an activity (ie. going out, doing sports, travelling)

☐[1] The entire baseplate had become detached

☐[1] The outer edge of the baseplate had become detached

☐[1] The center of the baseplate had become detached

☐[1] I was afraid the baseplate would become detached

☐ 1 The area around the stoma was itching

☐ 1 The area around the stoma was painful

☐ 1 There was leakage underneath **and** outside the baseplate

☐ 1 There was leakage underneath the baseplate (but not outside the baseplate)

☐ 1 The bag was full of air (ballooning)

☐ 1 There was a vacuum in the bag (pancaking)

☐ 1 Due to study visit

If 'Other reason for change', please specify: _____

After each test period:

Did you use any accessories in this test period?

☐ 0 No

☐ 1 Yes

If 'Yes' which accessories did you use? Please tick all that apply.

☐ 1 Adhesive remover (spray/wipes)

☐ 1 Paste

☐ 1 Rings

☐ 1 Ostomy tape

☐ 1 Ostomy belt

☐ 1 Hernia belt

☐ 1 Stoma powder

☐ 1 Barrier lotion/crème/spray/wipes

☐ 1 Cleansing wipes/cleansing spray

☐ 1 Odour remover

☐ 1 Other accessories. If 'Other' please specify: _____

Please indicate if you changed the use of accessories and in which way

	No change	Increased the amount	Decreased the amount
Adhesive remover (spray/wipes)	☐ 0	☐ 1	☐ 2
Paste	☐ 0	☐ 1	☐ 2
Rings	☐ 0	☐ 1	☐ 2
Ostomy tape	☐ 0	☐ 1	☐ 2
Ostomy belt	☐ 0	☐ 1	☐ 2
Hernia belt	☐ 0	☐ 1	☐ 2
Stoma powder	☐ 0	☐ 1	☐ 2
Barrier lotion/crème/spray/wipes	☐ 0	☐ 1	☐ 2
Cleansing wipes/cleansing spray	☐ 0	☐ 1	☐ 2
Odour remover	☐ 0	☐ 1	☐ 2
Other accessory	☐ 0	☐ 1	☐ 2

Safety endpoints:

Adverse events

7.1.3. Rationale for selection and measurement of end points

Trans Epidermal Water Loss (TEWL): TEWL is a standardized non-invasively method for describing the barrier function of the skin. Damage to the skin surface (stratum corneum) will lower the barrier of the skin and thereby increase the water loss. This can be used as a proxy for the damaging effects of the adhesive. TEWL is measured by applying a probe to the surface of the skin. The instrument is a DermaLab (Cortex Technology A/S, Hadsund).

[redacted]

[redacted]

7.1.4. Discussion of clinical investigation design

- Not possible to blind
- Open controlled using baseline data of current SenSura/SenSura Mio
- Test products will be compared to subject's own product
- Colostomy/Ileostomy subjects

In test period 2 using 14 test products, the subject has time to get used to handling the product as well as wearing the product and therefore the subject is qualified to answer questions as handling, comfort and preference. The subject will receive test products at the /cross-over visits.

7.2. Investigational device and comparator(s)

Subjects will minimum test 14 products ±1 product. Subject will however keep using the test products until next scheduled visit. Each subject will receive 1 box of 20 products at visit 3. The unused test products will after each test period be returned to the investigator/ investigator representative who will keep the accountability log up-dated. The subjects are not allowed to keep unused devices after study completion.

7.3. Subjects

To be included in the investigation, the subjects must comply with the selection criteria described in section 7.3.1 and 7.3.2.

7.3.1. Inclusion criteria for subject selection

Subjects interested in participating the clinical investigation must comply with the following criteria:

Inclusion criteria

To be included in the study the subjects must:	Justification for inclusion criteria:
1. Have given written informed consent and in DK: signed a letter of authority	To ensure voluntariness and in DK: that the Danish Medicines Agency have access to source data and/or data collected during the investigation in case of audit or inspection of data quality.
2.Be at least 18 years of age and have full legal capacity	To ensure that the subjects are competent and that data quality is high
3.Have had their colostomy/ileostomy for at least three months	To ensure that the initial post-operative problems are overcome, and that the subject are used to having an ostomy as well as changing the product before entering the investigation

4. Have a colostomy/ileostomy with a diameter between 10 and 55 mm	The CP Test product are only produced in a size that allows cutting the hole in the baseplate from 10 to 55 mm.
5.Be able to handle the Clinical App. and product themselves	In order to answer the CRF questions the subjects has to be able to handle the products themselves
6.Must be able to use custom cut product	To ensure products fits optimal around stoma. The study personnel must make sure that the subject knows how to cut the product in order for the base plate to fit optimal around the stoma.
7.Minimum change of product every second day	To ensure that subjects who changes their product every second day will test at least 14 products in the test period. Most 1-piece open users however change their products daily, i.e. these subjects will test at least 14 products in the test period.
8. Be willing to use Maxi bag during investigation	Only this bag size will be produced
9. Subject using Sensura or Sensura Mio flat 1 pc. open for at least two weeks before inclusion in the study.	To see changes from current product with a new top-film or adhesive and to ensure skin is in steady state.
10. Negative result of a pregnancy test for women of childbearing age (only DK)	Women of childbearing age must take a pregnancy test provided by the investigator before entering the study. The test shall show a negative result in order document that the subject is not pregnant.

7.3.2. Exclusion criteria for subject selection

Subjects complying with the following criteria must be excluded from participation in the clinical investigation:

Exclusion criteria

The subjects are not allowed to participate in case they: Justification for inclusion criteria:

1.Are currently receiving or have within the past 2 months received radio-and/or chemotherapy (low doses chemotherapy is allowed for other indications than cancer, e.g. below 15 mg methotrexate for rheumatoid arthritis)	The skin undergoes major changes because of radio-and/or chemotherapy, and therefore, the skin might be more fragile to product changes.
2.Are currently receiving or have within the past month received topical steroid treatment in the	Steroid product on peristomal skin may interfere with the skin condition. Use of steroid product can make the skin more fragile to baseplate change.

peristomal skin area, e.g. lotion or spray. Systemic steroid treatment (e.g. injection, or tablet) are allowed.	
3.Are pregnant or breastfeeding**	Even though the ingredients and the recipes have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
4. Are participating in other interventional clinical investigations or have previously participated in this investigation 4.1. Exception: Participation in other Coloplast in-house clinical investigations are accepted under the circumstances that the subject has paused the activities in the investigation and are otherwise complying with the inclusion and exclusion criteria of this (CP275) protocol.	Other interventional investigation guidelines/products may interfere with these investigational end points. Some of our studies are taking place over a two-year period, where the subjects will be paused for longer periods between the visits - therefore they are allowed to participate in other Coloplast studies meanwhile.
5.Are currently suffering from peristomal skin problems i.e. bleeding and/or broken skin (assessed by the investigator)	Class I devices must only be applied on intact skin, otherwise the device have to be up classified.
6.Have 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.

**ONLY APPLICABLE IN DK: Women are considered fertile as long as they have had a least one period during the last 12 months. Besides a negative pregnancy test the women must also sign a document claiming that they will use safe contraceptives during the study period (i.e. contraceptive coil, hormone base contraceptives or surgical sterilization). However, in some cases when the women are older than 50 years, but are not yet post-menopausal, the investigator may evaluate that it is not reasonable to ask these women to start using safe contraceptives for the duration of the investigation (e.g. if the subject is abstinent, the partner is surgically sterilized, or either subject or partner is infertile). In these cases the investigator can include the women, but has a responsibility of ensuring that he/she has done what he/she can to prevent these subjects from becoming pregnant. As a minimum investigator must talk to the women about the risk of and how to avoid unwanted pregnancy at inclusion and at every visit hereafter.

7.3.3. Recruitment and enrolment

[redacted]

The recruitment of potential subjects will commence only once authorisation has been received from the Regulatory Authorities and the EC. The subject invitation letter will be send to those subjects from the database that fulfils the criteria`s listed above.

Invitation Letters will be sent in two pools. First to potential subjects with an ileostomy and then potential subjects with a colostomy. This is to minimise the number of subjects inconvenienced with a run-in period and to minimise the use of a product other than their current product.

If a potential subject returns the reply letter to Coloplast, he/she will be contacted by phone.

If a potential subject is interested in participating, then written information about the investigation (subject information) will be sent to the subject to ensure that potential subjects are given the opportunity to read about the investigation before a possible informational visit, and so that they can prepare any possible questions they may have. The subject information provides information to potential 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 the potential subject is interested in participating in the investigation, a visit will be arranged in a room reserved for the purpose of ensuring privacy and quiet surroundings at the investigator's clinic/department, or at the home of the potential subject if he/she wishes. The subjects will receive both written and verbal information about the possibility of bringing a companion to the informational visit and to any possible subsequent visits. See section 14 for information to be given to the subjects, as well as the informed consent process. In addition to the informed consent form, the subject will have to sign a power of attorney, which permits the sponsor and the authorities to gain access to their medical records if necessary. Women of child-bearing age must sign a declaration that they will use a safe contraceptive throughout the entire investigation period. If a potential subject so desires, and it is certain that he/she has understood what the investigation entails and has signed the informed consent form as well as the power of attorney, he/she can continue directly to screening and inclusion as a continuation of the informational visit.

Subjects not currently using SenSura or SenSura Mio 1pc Open flat, but another flat product, will be asked if they are willing to use one of the products for 14 days before the inclusion visit (run-in period). If yes – they will be invited to a product screening visit, where a study nurse will check if or if not SenSura or SenSura Mio are suitable for the subject.

[redacted]

7.3.4. Subject withdrawal criteria

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

The investigator must withdraw a subject from the investigation for the following reasons:

- Non-compliance with the CIP impacting the scientific integrity of the investigation.
- If subject's safety and wellbeing is compromised by further participation
- If a subject withdraws or is excluded from the investigation, the data will still be recorded. Withdrawal subjects will not be replaced by new subjects.
- A subject who is withdrawn from the investigation, for any reason, will be encouraged to contact the investigator if problems arise that she/he believes are related to the investigation. A subject who has not experienced adverse events will not be followed up.
- For subjects who experience adverse events, see section 15.

7.3.5. Point of enrolment

A subject is considered enrolled in the investigation when the written informed consent and the letter of authority is obtained (Visit 0). The expected duration for each subject is described in section 7.1.

7.3.6. Total expected duration of the clinical investigation

[redacted]

7.3.7. Total number of subjects

Due to the explorative and qualitative nature of the test, 45 subjects based on a drop-out rate of 20% are considered sufficient to obtain the information needed and will give valuable feed-back for further development of ostomy products.

7.4. Procedures

7.4.1. Clinical investigation-related procedures

Before initiation of the clinical investigation, sponsor must be provided with key personnel's signed and dated curriculum vitae (not more than two 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.

Study information – Visit 0

Clinical site investigator and/or engaged clinical research professional (assigned investigator/study nurse) will introduce subject to the investigation.

If subject is currently using SenSura or SenSura Mio (1pc open flat) and wish to participate he/she can continue with the inclusion visit and visit 1, at the same day is possible.

Subjects not currently using SenSura or SenSura Mio (1pc open flat), but using another flat product, will be asked to continue the meeting with a product screening.

Product Screening (run-in period)
At the product screening the investigator or trained study nurse will decide, together with the potential subject, if SenSura and SenSura Mio (1pc open flat) could be suitable for the potential subject. If yes – the investigator or study nurse will decide which of the two products the subject should use as run-in product and therefore, if included, as own product (first test period). This decision is based on the fact that twice as many SenSura Mio users than SenSura users is needed in the study. Therefore, two-third users will be asked to use SenSura Mio in the run-in period and every third user will be asked to use SenSura in the ruin-in period. If the recruitment target is reached in one of the groups, following subjects will be asked to use the product where the recruitment target is not yet met. In addition, the subject will be informed about the run-in period.

If the subject wish to participate he/she can continue with the run-in period, and will be provided with products to use in this period.

Visit 0 - Inclusion Visit

If the subject wish to participate, fulfill the criteria for participation, and if consent is obtained the investigator and/or engaged clinical research professional (assigned investigator/study nurse) will enroll the subject in the study [redacted]

If the subject has participated in the run-in period, he/she will be provided with products to use as own product in the first test period.

Visit 1:

[redacted]

Testing: Own product (7 ±1 products). Subject will answer questions [redacted] used product at each product change.

Visit 2 (after using 5 products ±1 product **after conducting visit 1):**

[redacted]

Visit 3 (after using 7 products ±1 product **after conducting visit 1):**

[redacted]

Subjects are introduced to either test product 1, 2 or 3 depending on their usual product and randomization. Study procedures are introduced. Sufficient products are handed out to the subjects.

[redacted]

Visit 4 (after using 7 products ±1 product **after conducting visit 3):**

[redacted]

[redacted]

Visit 5 (after using 12 products ±1 product **after conducting visit 3):**

[redacted]

Visit 6 Completion/Termination (after using 14 products ±1 product **after conducting visit 3):**

[redacted]

[redacted]

The investigator/study nurse should encourage the subject to change his/her product as usual and not use his/her own product during test period 2.

Subjects are allowed to use all the accessories they normally use with their own product, such as paste,

protection film, lotion, powder and remover wipes/spray.

The Coloplast project team should be able to interview the subjects during the study if needed in a situation where the test products clearly do not perform as expected and/or at the last visit (visit 6).

If current product is not SenSura Mio or SenSura (1pc open flat) the Sponsor will provide the subject with products for both the run-in period and the first test period.

7.4.2. Activities performed by sponsor representatives

[redacted]

7.4.3. Foreseeable factors that may compromise the outcome / results

Use of ostomy accessories may influence the actual performance of the test products. It is not known if these accessories will have a "positive" or "negative" influence on the product performance. Some subjects entering the study may use accessories to minimize leakage under the base plate. When this is part of the subject's standard care procedure these subjects may continue to use the accessories, they used when entering the study if they use the same accessories throughout the entire study period i.e. for both products. It is important that a subject uses the same kind of accessories when testing the products as this gives the best conditions for comparing the performance of the products.

7.4.4. Flowchart

[redacted]

[redacted]

7.4.5. Randomisation Procedure

The subjects using SenSura Mio will be randomised to one of two treatment groups (same adhesive different top film or different adhesive same top film). [redacted]

[redacted]

7.4.6. Blinding

This investigation is not blinded, as it is not possible to blind the products due to visible differences.

7.4.7. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in the CRF.

The CRFs are printed and supplied by sponsor. A CRF is provided for each subject. It is the responsibility of the Investigator that all data are entered promptly and correctly.

Each CRF have printed instructions for completion.

[redacted]

[redacted]

7.4.8. Concomitant treatment

There is no mandatory concomitant treatment. Please see exclusion criteria`s for excluded medications.

7.5. Monitoring Plan

During the period of the investigation monitoring is carried out by a representative of sponsor according to the monitoring plan.
[redacted]
The CRF, questions in the clinical trial app, photo and video recordings and the declarations of informed consent and the letter of authority are source data. The informed consent forms, letter of authority, inclusion- and exclusion criteria and adverse events will be verified 100% to ensure that they have been completed correctly. All CRFs will be checked for missing or incorrect data. Furthermore, all events that arise during the investigation period will be recorded in the CRF and followed up by the investigator.

The CM is responsible for planning the monitoring.

The CM will have close contact with the investigator and the study nurse in the recruitment period to ensure that any concerns, problems or recruitment challenges are solved in a timely manner in conjunction with the site.

7.5.1. Source data verification

Assessments and observations during the investigation will be collected through five different methods:

- Paper CRF
- Clinical trial app
- Photos
- Video recordings
- Interviews (if applicable)

Case report forms in this investigation include the paper CRF and the clinical trial app. All of the above will be supplied by the sponsor.

The sponsor will be responsible for training the study nurse in completion of the paper CRF and the clinical trial app. The study nurse/Coloplast representative will instruct the subject carefully in completion the clinical trial app.

The questions in the clinical trial app will be completed by the subject, the baseline questions will be completed in collaboration with the study nurse. Subjects cannot make corrections in the clinical trial app once the data have been submitted.

The paper CRF will be completed by the study nurse. Any corrections in the paper CRF must be clearly signed and dated by authorised site personnel. The corrected entry must be crossed out so that the original entry is still legible.

CRF and clinical trial app and Informed Consent Forms; patient files may be source data for subject baseline characteristics, possible adverse events, serious adverse events, concomitant medication, concomitant disease and ostomy history.

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

7.5.2. Other methods for data quality assurance

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

8. Statistical considerations

8.1. Statistical design, method and analytical procedures

Definition of analysis populations

The ITT population (full analysis set) will be constituted by

all included subjects who:

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

Invalid individual data points may be omitted from analysis even though the corresponding subject is part of the ITT population. Any exclusion of data points will be documented.

The Safety population (basis for presentation of AEs) will constitute by subjects who have given informed consent.

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

Analysis of the primary endpoint

The primary endpoint is TEWL measured at 8 places (N, NE, E, SE, S, SW, W and NW) of the outer edge of the baseplate. The comparison in TEWL between the test products worn in the first and second test period is the primary objective of the investigation. This comparison will be made for all 3 arms. All TEWL data from the outer circle are analysed in a joint model.

A linear mixed model will be applied to the log transformed TEWL data. The model will include fixed interaction effects of arm (1,2,3) and product (in first and second period). Further the model will include:

- a random effect of subject

- a random interaction effect of product and subject
- a random interaction effect of position in the outer circle and subject
- a random interaction effect of visit, product and subject
- a random interaction effect of position, product and subject

As each endpoint is assessed three times for each position in the circle the model will also include a random interaction between subject, position, visit and product.

From this model the difference in TEWL between products in the first and second period will be estimated for each arm. As TEWL is analysed log transformed the estimated differences on log-scale will be back-transformed to the original scale as estimated ratios. Furthermore, the three arms will be compared.

Analysis of the secondary endpoint

Similarly, the difference in [redacted] in the outer circle between test products in test period 1 and 2 [redacted]

[redacted]

[redacted]

The endpoints regarding "Handling of base plate"("How did you find attaching the base plate?" and "How did you find detaching the base plate?") are assessed using an ordinal 5 point scales. A proportional odds model will be applied with the interaction between arm (1,2,3) and product (in first and second period) included as a fixed effect and with subject and the interaction between subject and product included as random effects. The odds ratio between the two test products as well as the corresponding 95% confidence intervals will be estimated for each arm, and a test of the hypothesis of no difference between test products (corresponding to an odds ratio equal to 1) will be performed for each arm. Other comparison within the model can be performed, if relevant.

The two endpoints regarding "Body fit/freedom of movements" will be analysed by the proportional odds model described above, if relevant.

[redacted]

All other endpoints will be listed or summarized by descriptive statistics.

Analysis of safety endpoints

Adverse events will be listed.

8.2. Sample size

The primary endpoint TEWL is measured at 8 positions (N, NE, E, SE, S, SW, W and NW, see figure in section 7) of the outer edge of the baseplate. For each subject 3 repeated measurements will be made for each position at 3 different days for both products worn in test period 1 and 2.

Part of the primary objective is to compare TEWL measured at the outer circle of the baseplate when wearing the 2 test products in each of the 3 arms.

As the variation between days (visits) and positions are unknown the sample size is based on a simplified model with variation comparable to what was observed in CP254. The simplified model corresponds to comparing the 2 test products with 3 repeated measurements at one visit for one position. A large variation between

test visits will decrease the power. The three repeated measurements taken on three different visits will however limit the impact the different visits haves on the power. Furthermore, measurements are performed at 8 different positions in the outer circle this is likely to increase power.

Based on data from CP254 study it is assumed that the standard deviation of log-transformed TEWL (log(TEWL)) is 0.62. Further it is assumed that the correlation between the three repeated measurements of log(TEWL) assessed at the same position is 0.62, whereas the correlation between repeated measurements corresponding to two different test products is 0.27. In the below table the needed sample size is seen for varying values of the true ratio in TEWL and for different values of the power to demonstrate that the ratio is significantly different from 1 (that the 95% confidence interval excludes 1).

Table: Subjects needed for test of each test product within an arm on peristomal skin.

	Power		
True TEWL Ratio	0.8	0.85	0.9
1.6	16	17	19
1.7	12	14	16
1.8	11	12	13
1.9	9	11	11
2.0	8	9	10

Based on these numbers 12 subjects should test each test product in order to ensure a power of 80% if the true ratio between subject's current product and the test product is 1.7. To take a potential drop-out into account it is recommended to include a total of 15 subjects in each arm, resulting in a total of 45 subjects.

With 12 subjects in each arm there are 87% power to detect a true TEWL ratio of 2.2 between the test product ratios in 2 different arms (where TEWL measured on the subjects are not paired).

8.3. Level of significance and power

Statistical tests will be carried out as two sided tests on a 5% level of significance. For information regarding the power, see the above section

8.4. Drop-out

It is assumed that 20% of the subjects may drop out during the investigation. To ensuring 12 completers in each arm, 15 subjects will be allocated to each of the 3 arms, adding up to a total of 45 subjects

8.5. Pass/fail criteria

No formal success criteria are applied in this explorative investigation. The investigation will provide valuable insight into how the peristomal skin react if the topfilm on existing ostomy products is changed to a softer topfilm or the adhesive is changed but the topfilm is the same on an existing product.

8.6. Interim analysis

The sample size calculation (see section 8.2) was performed in a simplified model without an assumed variance component for variation between visits and position of measurements as the variation was unknown at the time of sample size calculation. After including part of the planned subjects, it is possible to get an estimate of the variance components. Hence, an interim analysis will be performed to get an estimate of the variance components and a better estimate of the total variation after at least 8 finalized subjects in each arm. If the results of the interim analysis show less variation than assumed in the sample size calculation and/or a higher TEWL ratio than assumed, then it may be possible to show significant difference between the test products with a smaller sample size. If it is possible to evaluate how the peristomal skin react if 1) the topfilm on existing ostomy products is changed to a softer topfilm or 2) the adhesive is changed but the topfilm is the same, based on the interim results, the recruitment will be stopped to avoid unnecessary inconvenience for subjects.

The interim analysis will be performed in a population that fulfill the ITT criteria by the trial statistician as this is an exploratory investigation and the results only will be used for internal decision making.

The interim analysis will consist of:

- Analysis of primary endpoint: TEWL
- [redacted]

[redacted]

[redacted] Statistical reason for termination of investigation

If the results of interim analysis are sufficient for evaluating the objective of the exploratory study the recruitment of subjects will be stopped

8.8. Deviation(s) from statistical plan

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

9. Data management

9.1. Data review, database cleaning, and issuing and resolving data queries

Data management and statistical analyses is carried out by the Medical Affairs, Coloplast A/S.

To ensure correct data entry, data from CRF is entered twice (double data entry). Data management is responsible for control of data consistency and also for completeness of data from each subject.

Discrepancies are listed in Data Query Forms (DQF), and the Investigator is responsible for solving these promptly. When all DQFs are solved the database is locked and the statistical analyses are performed.

9.2. Verification, validation and securing of electronic clinical data systems

EXPeRT Data Management, version 5.0.05 system delivered by OmniComm Systems Inc. is used for data management. The system is designed to be compliant with the requirements of 21 CFR part 11. It is a validated data management system allowing only qualified and trained personnel to enter the system.

For collection of the patient diary data, Coloplast A/S uses a newly developed clinical trial application delivered by “Blue Fragment”.

9.3. Data retention

The sponsor file must be archived for a minimum period of 5 years after the final clinical investigation report has been signed.

All investigation site documents must be archived for a minimum period of 5 years after the final clinical investigation report has been signed. The monitor is responsible for informing the investigator and the CTM if this period should be longer for their sites according to local regulation.

10. Amendments to the CIP

Any significant changes to the CIP must be:

- Agreed between the sponsor and the investigator
- Justified in a statement included in the amended section. The version number and date of amendment must be documented
- Registered in the Change Log
- Notified to or approved by the Ethical Committee of the Capital Region of Denmark before implementation
- Notified to or approved by the Danish Medicine Agency before implementation

Examples of significant changes include: changes to inclusion criteria, endpoints or assessment methods.

11. Clinical Investigation Plan deviations

The investigator is not allowed to deviate from the CIP unless under emergency circumstances and to protect the rights, safety and well-being of the subject(s). Deviations must be reported to the sponsor and deviations affecting the scientific aspect of the investigation or the safety of the subject are reported to the Ethical Committee of the Capital Region of Denmark and Danish Medicine Agency by the sponsor, if required.

Definition of deviation:

Deviations are changes that affect the rights, safety and well-being of the subject(s), e.g. missed informed consent, an enrolled subject that does not fulfil the inclusion criteria or a serious adverse event that is not reported to the sponsor.

Minor deviations could include administrative changes, change of monitor(s), changes to telephone numbers, and renewal of insurance.

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

12. Device Accountability

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

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

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

- Date of receipt
- Identification of each investigational device (lot number)
- The expiry date
- The date of return of unused, expired or malfunctioning investigational devices
- Subject identification

13. Statement of compliance

The clinical investigation is conducted in accordance to:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Seoul, October 2008.
- MDD 93/42/EEC as amended by Directive 2007/47/EC (commonly known as the Medical Device Directive).
- ISO 14155:2011 “Clinical Investigation of medical devices for human subjects – Good clinical practices”.
- Any applicable regional or national regulations will be specified in the country specific CIP.
- Executive Order on Medical Devices no. 1263 of 15 December 2008 (Bekendtgørelse om medicinsk udstyr nr. 1263 af 15. december 2008)
- EC Directive 95/46/EF regarding data protection, Jan. 2012
- Act of processing of Personal data Act. no. 429 of 31 May 2000

13.1. Ethics committee and regulatory authorities

The CIP and/or other relevant documents are submitted to the appropriate EC(s) and regulatory authorities. This clinical investigation will not begin until the required approval from the EC and regulatory authorities have been obtained. Any amendment to the protocol will be submitted to the same EC(s) and regulatory authority. Sponsor will notify the relevant regulatory authority and EC(s) concerned of the end of the clinical investigation. Approval from the Danish Protection Agency is not necessary as this clinical investigation is done by a private company and therefore is exempted from notification.

13.2. Data protection

Information about subject identity is filed as a confidential document by the investigator(s) and subjects are referred to only as numbers on all other documents. The data is blinded correspondingly in the data analysis.

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

13.3. Indemnity

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

XL Insurance Company SE
Kungsgatan 5, 2nd floor
SE-111 36 Stockholm
Phone +46 8 440 89 80
Policy number: DK00000300LI16A

13.4. Financial conditions

The clinical investigation is initiated and sponsored by Coloplast A/S.

14. Informed consent process

Written informed consent is obtained from all subjects participating in the following detailed written and verbal briefing.

The informed consent process takes place in a room reserved for the purpose of ensuring privacy and quiet surroundings at the investigator's department. The subjects will receive both written and verbal information about the possibility of bringing a companion to the visit and to any possible subsequent visits. If he decides to participate in the study, he signs the written informed consent form.

The investigator, or study nurse, provides a non-technical version of the information to the subject in native language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks or inconveniences and/or expected benefits. Subjects will have time to ask questions and have a minimum of 24 hours before deciding on whether or not to participate in the investigation. If the subject wishes to consent immediately after receiving information, he may do so and in- and exclusion may be initiated. Subjects will be informed that their participation is voluntary and that they may leave the investigation at any time, without influencing any current or future treatment they may have outside this clinical investigation.

Those who decide to participate will be asked to fill out an informed consent form, which the investigator or study nurse and subject will sign and date. He will also be asked to fill out the letter of authority, giving representatives from Coloplast A/S, Investigator, Danish Medicine Agency and possible third countries access to relevant data registered in the investigation. The subjects will be given a copy of the signed informed consent form and letter of authority.

If the subject in the Informed Consent Form has accepted that his personal physician may be informed about his participation in the study, a letter stating this will be sent by the investigator or study nurse to the personal physician with the purpose of adding this to the subjects' patient record. If the subject has not accepted that his personal physician is informed, he may be included anyway. This is considered acceptable as investigator informs the subject to contact him should an adverse event occur.

If new information becomes available during the investigation, the sponsor will inform the investigator, and the new information will be provided to the subjects by the investigator. If new information becomes available that can significantly affect a subject's future health and medical care, the information will be provided to the subjects in written form. The clinical manager is responsible for producing the written information and providing it to investigators who will provide it to the subjects. If applicable, all affected subjects will be asked to confirm their continued informed consent in writing.

15. Adverse events, serious adverse events and device deficiencies

15.1. Adverse events

15.1.1. Adverse event

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.

15.1.2. 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, malfunction of the device, use error or from intentional misuse of the device.

Table 2 lists anticipated adverse device effects that may occur.

Table 2 Anticipated adverse device effects and their likely incidence rates

ANTICIPATED ADE	INCIDENCE RATE
Peristomal skin irritation (incl. mechanical trauma)	[redacted]
Allergic peristomal skin irritation (dermatitis)	

Temporary redness upon removal of the base plate is not considered an adverse device effect, however an abnormal development in intensity or duration should be considered as such.

15.2. Device deficiency

A device deficiency is the inadequacy of the investigational medical device with respect to its identity, quality, durability, reliability, safety or performance. This includes malfunctions, misuse or use errors and inadequate labelling.

Primary and secondary endpoints that are measured during this investigation will not be required to be reported as device deficiencies.

15.3. Serious adverse events

15.3.1. Serious adverse event

A serious adverse event is an adverse event that:

- Led to death,
- Led to a serious deterioration in health of the subject that either resulted in:
  1) a life-threatening illness or injury, or
  2) a permanent impairment of a body structure or a body function, or
  3) required in-patient hospitalization or prolongation of existing 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.

15.3.2. Serious adverse device effect

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

15.3.3. Anticipated serious adverse device effect

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.

15.3.4. Unanticipated serious adverse device effect

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.

15.4. 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.

15.5. Reporting and timelines

15.5.1. Investigators reporting responsibilities

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

- All serious adverse events and serious adverse device effects must be reported to sponsor within 2 working days.
- 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 2 working days.
- New findings and/or updates in relation to already reported serious events should also be reported to sponsor within working 2 days.
- Device deficiencies and all adverse device effects must be reported to sponsor within 10 days.

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

[redacted]

[redacted]

15.5.2. 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.

Sponsor must inform all investigators in writing within ten days after the sponsor is made aware, if an (S)AE or Device Deficiency led to corrective actions (e.g change of IFU)

16. 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).

17. Clinical investigation report

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

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

The clinical investigation report must be submitted to EC and regulatory authorities (if relevant)

18. Publication policy

18.1. General

In connection with the publication policy Coloplast is referring to the internal document 'Clinical Publication Practice' that will be available for internal and external persons involved in the publication process.

The results of the investigation, positive as well as negative and inconclusive will be registered and published on clinicaltrials.gov webpage. The subjects' identity will remain confidential. The results will not be submitted to a scientific journal. Publication of results on the webpage will be initiated as soon as scientifically acceptable and according to the law of personal data protection (Lov om behandling af Personoplysninger), however within one year after the last subject has completed the investigation. Data from the investigation is considered confidential until it is published according to the conditions of this CIP and the 'Clinical Publication Practice'. Sponsor may publish anonymous single subject case stories (or public, if the subject consents) at any time during and after the investigation.
Sponsor reserves the right to use the data (published and unpublished) for reimbursement or regulatory purposes.

19. Bibliography

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[3] Product Risk Assessment CP275 Veeva no.: VV0128400

[4] Biological Evaluation Report CP275 Veeva no.: VV0127825

[5] Investigators Brochure CP275 Veeva no.: VV0127486