Clinical Investigation Plan

CP288

Investigation of a new stoma product for people with a stoma

January 2020 – May 2020

NCT04101318

Document date: 2019Sep02

[redacted]

CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	Document established based on template 7.0

[redacted]

Table of Contents

1. Sponsor representatives 10

1.1. Principal Investigators 10

1.2. Other vendors 11

2. Rational and justification for conduct of the clinical investigation 11

3. Aim and Objective(s) for the clinical investigation 11

4. Design of the clinical investigation 12

4.1. General 12

4.2. Total expected duration of the clinical investigation 13

4.3. Discussion of clinical investigation design 13

4.4. Endpoints 14

4.4.1. Primary endpoint 14
4.4.2. Secondary, explorative and safety endpoints 14
4.4.3. Rationale for the selection of endpoints 14
4.4.4. Baseline data 14

4.5. Randomisation Procedure 15

4.6. Blinding 15

5. Investigational products 16

5.1. The non-CE marked Investigational product 16

5.1.1. Description of the non-CE marked investigational product 16
5.1.2. Manufacturing 16
5.1.3. Intended purpose of the investigational product in the clinical investigation 16
5.1.4. Intended population for the investigational products 16
5.1.5. Instruction for use 17
5.1.6. Total number of investigational products intended for the clinical investigation 17

5.2. Comparator investigational product(s) 17

6. Clinical Investigation population 18

6.1. Eligibility criteria 18

6.1.1. Inclusion criteria 18
6.1.2. Exclusion criteria 19
6.1.3. Pregnancy and breastfeeding 20

6.2. Recruitment and enrolment 20

6.3. Subject withdrawal/lost to follow up criteria 22

6.3.1. Screening failures 22

6.4. Point of enrolment 22

6.5. Subject Identification and confidentiality 22

7. Procedures 23

7.1. Clinical investigation-related procedures 23

7.1.1. Site visits 23
7.1.2. Visit calls 24
7.1.3. Product change 24

[redacted]

7.1.4. Safety 24
7.1.5. Follow-up after the investigation 24
7.1.6. Interview 24
7.2. Flow-chart 25
7.3. Case Report Forms 26
7.4. Concomitant treatment 26
8. Risk – benefit analysis 26
8.1. Risk-benefit analysis of the Coloplast investigational product 26
8.2. Risk-benefit analysis for the conduct of the clinical investigation 27
9. Monitoring 27
9.1. Periodic Monitoring visit(s) 28
10. Source data verification 28
11. Statistical considerations 29
11.1. Statistical design, method and analytical procedures 29
11.2. Sample size 31
11.3. Level of significance and power 31
11.4. Pass/fail criteria 32
11.5. Interim analysis 32
11.6. Statistical reason for termination of investigation 32
11.7. Deviation(s) from statistical design, method or analytical procedures 32
12. Data collection and data management 32
12.1. Data Collection in the clinical investigation 32
12.2. Database Management and Quality Control 32
12.3. Data review, database cleaning, and issuing and resolving data queries 33
12.4. Data retention 33
13. Amendments to the CIP 33
14. Deviations from Clinical Investigation Plan 34
15. Accountability of investigational products 34
16. Statement of compliance 35
16.1. Ethics committee and regulatory authorities 35
16.2. Data protection 35
16.3. Financial conditions 36
16.3.1. Investigator payment 36
16.3.2. Subject compensation 36
16.3.3. Compensation in case of injury 36
17. Informed consent process 37
18. Adverse events, adverse device effects and device deficiencies 37

[redacted]

18.1. Adverse events **37**
18.2. Adverse device effect **37**
18.2.1. Anticipated device effects 37
18.3. Device deficiency **37**
18.4. Serious adverse events (SAE) **38**
18.4.1. Serious adverse device effect (SADE) 38
18.4.2. Anticipated serious adverse device effect (ASADE) 38
18.4.3. Unanticipated serious adverse device effect (USADE) 38
18.5. Medical care of subjects **38**
18.6. Reporting and timelines **39**
18.6.1. Investigator's reporting responsibilities 39
18.6.2. Sponsors reporting responsibilities 39
18.6.2.1 Medical Advisor Safety Review 40
18.6.2.2 Data Safety and Monitoring Board 40
19. Suspension or premature termination of the clinical investigation ***41***
20. Clinical investigation report ***41***
21. Publication policy ***41***
22. Appendix ***42***
22.1. Appendix 1 - Endpoints **42**
22.2. Appendix 2 – Leakage scale questionnaire **58**
22.3. Appendix 3 - Quality of life questionnaire **59**
22.4. Appendix 4 – Baseline data **60**
22.5. Appendix 5 - Bristol scale **62**
22.6. Appendix 6 – Classification of leakage **63**

[redacted]

SYNOPSIS OF THE CLINICAL INVESTIGATION

Title

CP288 - Investigation of a new stoma product for people living with a stoma.

Test products and comparator:

The CP288 Coloplast investigational products are non-CE marked stoma products based on the [redacted] and a [redacted] products to which comprises of a [redacted] The comparator products are considered Standard of Care or products considered to be part of Standard of Care in coming years, and include:

1-piece [redacted]

2-piece [redacted]

They are considered the newest products launched by the largest manufacturers covering the majority of the market.

Intended purpose

The product is intended to support collection of output from a stoma and to provide a [redacted] between peristomal skin and stomal output.

Aim and objective(s)

The **aim** of this investigation is to investigate the performance and safety of a new baseplate [redacted] which is expected to reduce peristomal skin complications induced by output.

The primary objective is to investigate whether a new baseplate with a [redacted]

The secondary objective is to evaluate the [redacted] for the peristomal skin condition.

Design of the investigation

This investigation is a randomised, controlled, open-label, comparative, cross-over, multicentre investigation, with two test periods. In total, 96 subjects will be included and randomised, and each subject will have three test visits overseen by the Principal Investigator, or delegate. Each subject will be enrolled for $2 \times 42^{\pm 3}$ days in total for the entire investigation, thus for a maximum of 90 days. The subjects will test the non-CE marked Investigational product and one of the five comparator investigational products in randomised order.

Expected duration of the clinical investigation:

The investigation will be conducted in January 2020 through May 2020.

Primary endpoint

- Max itching score within a week at steady state

For Secondary and explorative endpoints please see Appendix 1 - Endpoints.

[redacted]

Population/subjects

Subjects with an ileostomy or colostomy with liquid output, currently using a flat (e.g. non-convex/concave) baseplate.
To take a potential drop-out (20%) into account it is recommended to include a total of 48 1-piece and 48 2-piece users, resulting in a total of 96 subjects included and randomised.
The subjects will be included by competitive recruitment in up to 15 sites in five different countries (UK, Germany, the Netherlands, Italy and Norway).

Investigation approval

The investigation will be approved by the Ethical committees/IRB and the regulatory authorities in the participating countries (The Netherlands, United Kingdom, Italy, Germany and Norway) before investigation initiation.

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 18.2
AE	Adverse Event	See section
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	
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
	Steady state	
USADE	Unanticipated Serious Adverse Device Effect	See section 18.4.3

[redacted]

> SIGNATURE PAGE

All parties declare by their signature on the electronic or the separate signature page to follow the Clinical Investigation Plan CP288 in accordance with the Declaration of Helsinki, ISO 14155 and the Medical Device Directive/Medical Device Regulation.

[redacted]

1. Sponsor representatives

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

COORDINATION CLINICAL MANAGER	STATISTICIAN
[redacted]	[redacted]
CLINICAL MANAGER	**CLINICAL MANAGER**
[redacted]	[redacted]
SCIENTIFIC MANAGER	**PROJECT MANAGER**
[redacted]	[redacted]
DATA MANAGER	**HEAD OF CLINICAL OPERATIONS**
[redacted]	[redacted]
MEDICAL ADVISOR	
[redacted]	

In case of emergency, please contact the coordinating clinical manager [redacted]

1.1. Principal Investigators

This clinical investigation involves up to 15 sites in five different countries; United Kingdom, Germany, Italy, The Netherlands and Norway.

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

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 delegates will receive training in all aspects of the investigation and before they can begin any

[redacted]

investigational related tasks. The training must be documented in the 'Clinical Investigation Training Log' at each site. The PI is responsible for maintaining these logs.

1.2. Other vendors

Clinical Research Organizations (CROs) may be used to help conduct the investigation as Sponsor representatives in one or more countries. The CROs, their role and responsibilities will be listed in the 'Site Personnel and Contact Details List'.

The company [redacted] will help with the validation of the [redacted]

2. Rational and justification for conduct of the clinical investigation

People with intestinal stomas (especially ileostomists) have, despite development of better stoma products, problems with leakage induced peristomal skin complications which influence quality of life negatively[1][2]. To overcome this, Coloplast A/S has developed a [redacted]. The aim is to evaluate of whether the new baseplate can reduce peristomal skin complication induced by output.

3. Aim and Objective(s) for the clinical investigation

The **aim** of this investigation is to investigate the performance and safety of a new baseplate [redacted] which is expected to reduce peristomal skin complications induced by output.

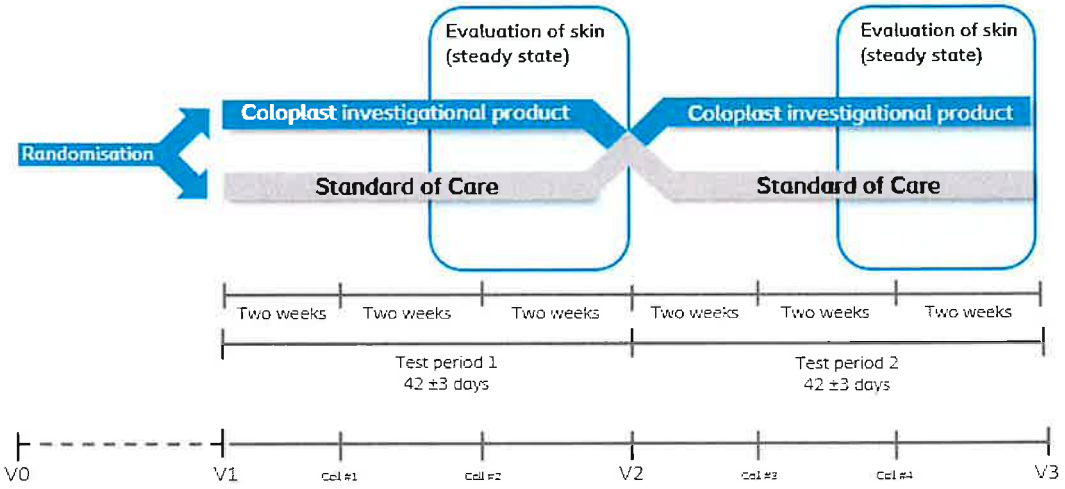
The primary objective is to investigate whether a new baseplate [redacted] can reduce peristomal skin complications induced by output.

The secondary objective is to evaluate the [redacted] for the peristomal skin condition.

[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] 5] 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

4. Design of the clinical investigation



4.1. General

This investigation is a randomised, controlled, open-label, comparative, cross-over, multicentre investigation, with two test periods. In total 96 subjects will be included and randomised, and each subject will have three test visits overseen by the Principal Investigator, or delegate. Each subject will be enrolled for $2 \times 42^{\pm 3}$ days in total for the entire investigation, thus for a maximum of 90 days. The subjects will test the Coloplast investigational product and one of the comparator products in randomised order.

Before the test periods, the subjects are invited for an information and inclusion visit (V0). Subjects sign all consent forms at the visit before continuing the investigation. During their participation the subjects will complete three test visits (V1, V2 and V3). The visits can be at the Principal Investigators clinic or in the subject's home depending of the nature of the site. In addition, the Principal Investigator, or delegate, will call the subjects every second week during the test periods, thus four phone calls during the investigation.

During the test visits both the subject and the Principal Investigator, or delegate, will complete questionnaires about the subjects peristomal skin condition, the stoma, use and handling of the products, leakage, quality of life and preference, and discuss/record any adverse events.

At every product (1pc) or baseplate (2pc) change the subjects will be asked to take photos of their stoma and peristomal skin and the backside (adhesive side) of the used product with a Clinical Trial App in a smartphone.

Coloplast will provide both the test product and the comparator product for all subjects via the Principal Investigator, based on the subject's usual changing pattern.

If a subject experiences problem with one of the investigational products during the investigation, he/she should contact the investigator for advice. The investigator may reschedule the next visit, e.g. to move it forward to resolve the issue or to monitor an AE. Subjects that can/will not complete a test period with a test product may move forward to the next visit and test period instead of dropping out of the investigation. In this case, the subject may use his/her own product until the next visit. However, this must be documented by the Principal Investigator. The next visits should be scheduled as soon as possible.

[redacted]

Please see section 7(Procedures) for more information about procedures during the investigation.

4.2. 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.

- First subject enrolled (January - 2020).
- Last subject enrolled (February - 2020).
- Last subject completed (May - 2020).
- Final report (November - 2020).

4.3. Discussion of clinical investigation design

The open-label, randomised, controlled, comparative, cross-over design was selected for CP288 based on the following advantages:

Randomised:
- The randomisation ensures that the study effect, including selection bias and confounding covariates are adjusted for.

Cross-over:
- The influence of confounding covariates is reduced because each cross-over subject serve as his or her own control.
- Cross over design allows us to assess user preference as all users will try both the new non-CE marked product and one of five CE marked products
- Subjects are their own control and fewer subjects need to be included, even though the test period is longer.
- Requires fewer subjects than parallel designs.

Open label:
- The investigation is not blinded because the Coloplast investigational product and comparators are visibly different from each other.

Enrolment period:
- The duration of the test periods ($42^{\pm 3}$ days) and number of visits should be adequate to assess data on the wear time, leakage pattern, and skin condition of the subjects. The investigational products are tested for $42^{\pm 3}$ days to ensure that the skin will have time to adjust to new conditions, reach a steady state, and for the subjects to test an adequate number of products to give a thorough evaluation of the products.

To account for a possible carry-over effect the steady state period of the of the treatment period begins after three weeks of product use as it is anticipated that the skin has adapted to the new product after three weeks. The statistical analysis will evaluate if there are signs of a carry-over effect and take that into consideration when presenting the results.

4.4. Endpoints

Primary, secondary and explorative endpoints are mentioned on a high level. Endpoint details and flow-chart of measures are presented in Appendix 1 - Endpoints, Appendix 2 – Leakage scale questionnaire and Appendix 3 - Quality of life questionnaire.

4.4.1. Primary endpoint

- Maximum itching score within one week at steady state

4.4.2. Secondary, explorative and safety endpoints

Mentioned by group name.

Secondary endpoints	Explorative endpoints	Safety endpoints
- Itching - Pain - Burning - Bleeding/ Weeping or moist skin/Ulcers or sores - Overall physical discomfort - Overall ability to move around - Overall ability to stick the stoma bag adhesive to your skin - Discoloration - Intensity - [redacted]	- Stoma behaviour - Feeling of security - Handling - Leakage - Quality of life - Preference - Reason for change - Use of accessories - Ballooning	- Adverse events - Device deficiencies

4.4.3. Rationale for the selection of endpoints

The skin endpoints are subjective and objective parameters describing the health of the peristomal skin. Therefore, these are essential to investigate if the new baseplate [redacted] can reduce peristomal skin complications induced by output.

[redacted] the baseplate and the possible effect [redacted] could affect feeling of security, leakage, handling, wear time and quality of life and are reasons why associated exploratory endpoints are assessed in this investigation.

Adverse events and device deficiencies comprise safety parameters.

4.4.4. Baseline data

Baseline data are mentioned on a high level. Endpoint details and flow-chart of measures are presented in Appendix 4 – Baseline data. The data are registered at the first test visit (V1) by Principal Investigator, or a delegate.

- Inclusion and randomisation data
- Demographics
- Stoma information
- Current product usage
- Changing routine
- Peristomal skin area
- Assessment of body profile
- Frequency of skin complications
- Treatment of skin complications
- Leakage

4.5. Randomisation Procedure

All subjects that meet the inclusion and exclusion criteria will be randomised to one of two treatment arms. Each arm examines the non-CE marked investigational product and one of the CE marked comparator investigational products in the following order:

- Arm A: The non-CE marked investigational product, then one of the five CE marked comparators investigational products.

- Arm B: One of the five CE marked comparators investigational products, then the non-CE marked investigational product.

There will be one randomisation list for the subjects normally using a 1-piece product and one for subjects normally using a 2-piece product. This is to stratify the two types of subjects to the treatment arms. The randomisations list will consist of blocks of ten, and centralised.

4.6. Blinding

No blinding will be used in this investigation, as it is not possible to blind the products due to visible differences.

[redacted]

5. Investigational products

5.1. The non-CE marked Investigational product

5.1.1. Description of the non-CE marked investigational product

[redacted]

Table 1: Overview of product specifications for the non-CE marked investigational product

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

5.1.2. Manufacturing

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

5.1.3. Intended purpose of the investigational product in the clinical investigation

The non-CE marked investigational product is intended to support collection of output from a stoma and to provide a [redacted] between peristomal skin and stomal output.

5.1.4. Intended population for the investigational products

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

5.1.5. Instruction for use

The handling of the non-CE marked investigational product 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 delegates will receive training by the sponsor and/or principal investigator in the handling and correct use of the investigational products. The Principal Investigator, or delegate, will train the subjects in the correct use of the test products.

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

The subjects will be included for $42^{\pm 3}$ days per test period, for a total of up to 90 days.

Subjects using 1-piece products are expected to change their products every day. Therefore, they are expected to use 45 test products and 45 comparator products during their participation.

Two-piece users are expected to use two baseplates every three days. Therefore, they are expected to use 30 test product baseplates and 30 comparator baseplates during their participation.

5.2. Comparator investigational product(s)

The following comparator products has been chosen for this investigation:

1P:

[redacted]

2P:

[redacted]

The comparator investigational products are considered Standard of Care or products considered to be part of Standard of Care in coming years, and therefore the newest products launched by biggest manufacturers covering the majority of the market.

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

[redacted]

6. Clinical Investigation population

Based on the sample size calculation (see section 11.2) 48 1-piece and 48 2-piece users should be included and randomised.

The subjects will be included by competitive recruitment in up to 15 sites in five different countries (UK, Germany, the Netherlands, Italy and Norway.

6.1. Eligibility criteria

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

6.1.1. Inclusion criteria

Inclusion criteria	To be included in the investigation a subject must comply with the following inclusion criteria:	Justification for inclusion criteria
1.	**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 participation
2.	**Has an ileostomy or colostomy with liquid output*** ***Definition of liquid output: Six-Seven in the Bristol scale** (Appendix 5 - Bristol scale)	The product is indicated for use with surgically ileostomies and colostomies with liquid output.
3.	**Currently using a flat product**	The test product is a flat (i.e. non-convex or non-concave) product
4.	**Be at least 18 years of age and have full legal capacity**	To meet the Helsinki Declaration
5.	**Have had their stoma for at least three months (90 days)**	To ensure that the initial post-operative problems are overcome, and that the subject are used to having a stoma as well as changing the product before entering the investigation
6.	**Can use a product with a max cut size of 40 mm**	The cut max of one comparator is 40 mm.
7.	**Has experienced leakage* under the baseplate at least three times within the last fourteen days.** ***Leakage defined as output seeping under the baseplate** (Appendix 6 – Classification of leakage)	To ensure that the user has potential leakage induced skin complications
8.	**Has symptoms of peristomal skin complications or has peristomal skin complications defined by at least one of the below** a) Has experienced symptoms of skin complications (itching, burning, pain) within the last fourteen days b) Has experienced red skin in the inner circle (within three cm from stoma edge) within the last fourteen days c) Has skin complication (assessed by Principal Investigator, or delegate) in the inner circle (within three cm from stoma edge) of the peristomal area	To ensure that the user has skin complications in the peristomal area.
9.	**Is able to handle the electronic diary (questionnaire/photo) themselves**	To answer the CRF questions and take photo the subjects must be able to handle the electronic diary themselves.

[redacted]

Inclusion criteria To be included in the investigation a subject must comply with the following inclusion criteria:		Justification for inclusion criteria
10.	**Is able to handle (apply, remove, cut etc.) the product themselves**	The subjects must be able to handle the product/baseplate themselves to evaluate the handling of the product, which is an endpoint in this investigation.
11.	**Is willing to not use barrier film or barrier cream during the investigation**	The use of barrier film or cream could compromise the effect of the new baseplate
12.	**Is willing and suitable (determined by Principal Investigator, or delegate) to use a flat custom cut one-piece open or a two-piece open product during the investigation.**	To ensure compliance with the protocol during the investigation
13.	**Is willing to change the product (1pc) or baseplate (2pc) at least every fourth days.**	To ensure enough changes is recorded in the CRF

6.1.2. Exclusion criteria

Exclusion criteria A subject is not allowed to participate in case he/she:		Justification for exclusion criteria:
1.	**Is currently receiving or have within the past 60 days received radio-and/or chemotherapy** - low doses chemotherapy (assessed by Principal Investigator) is allowed for indications other than cancer	The skin undergoes major changes because of radio- and/or chemotherapy, and therefore, the skin might be more fragile to product changes.
2.	**Is currently receiving or have within the past month 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 Principal 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.
3.	**Is breastfeeding**	Even though the ingredients and the recipes have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
4.	**Is pregnant (based on pregnancy test - urine)**	Even though the ingredients and the recipes have been approved for humans, their effect on embryos, foetuses, and infants are unknown.
5.	**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.

[redacted]

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 (V0) after signed informed consent, to ensure the subject is not pregnant. The urine pregnancy test will be performed by dipstick at the investigation site. Furthermore, the female subjects should not be breastfeeding, when participating in the clinical investigation.

Principal Investigator must talk to the women about the risk of and how to avoid unwanted pregnancy at inclusion and at every test period the subject participates in hereafter.

If the subject is sexually active, she should be willing to practice appropriate contraceptive methods until the end of the investigation.
Appropriate contraceptive methods are:

- sexual abstinence (in some cases when the women are older than 50 years, but are not yet post-menopausal, the Principal Investigator may evaluate that it is not reasonable to ask these women to start using safe contraceptives for the duration of the investigation)
- oral contraceptives
- trans dermal patches
- depot injection of a progestogen drug
- double barrier method
- condom or occlusive cap (diaphragm or cervical/vault caps) plus spermicidal agent
- intrauterine device (IUD)
- intrauterine system (IUS)
- implant, or vaginal ring (placed at least 4 weeks before the first test period
- male partner sterilisation before the female participant's entry into the investigation and is the sole sexual partner for that female participant.

However, national requirements should always be followed.

If the subject becomes pregnant during the investigation, it is important, that the subject informs the Principal Investigator, or delegate, immediately. Hereafter the subject will be withdrawn from the investigation.

6.2. Recruitment and enrolment

The recruitment of potential subjects will commence only once authorisation has been received from the Regulatory Authorities and the EC.

Table 2: Table showing an overview of the recruitment process

Recruitment method	**Coloplast Database**	**Advertisement**	**Patient records**
Potential subjects	Recruitment will go through Coloplast' own subject database (stoma care users), and a "landingpage" at Coloplast website. Potential subjects are identified by the following searching criteria in the Coloplast database: • Has an ileostomy or colostomy	Advertisement i.e. in local shops, sports facilities, local newspapers, social media and stoma associations. The advertisement will state the contact information of relevant Principal Investigator(s) to contact or the web-address for a Coloplast 'recruitment landing page'. A CRO may help by receiving reply	Recruitment from hospitals, home care nurses and outpatient stoma clinics will be via patient visit or screening of subject records kept at the participating sites.

[redacted]

	• Be at least 18 years of age	letters/mails and/or answering the phone from interested subjects.	
First contact	The identified potential subjects will as first contact be sent an Invitation and Reply Letter by mail or email.	Interested subject contact the investigator.	The identified potential subjects will be contacted and informed about the investigation by the investigator (via telephone, letter or e-mail).
	If a potential subject does not return the reply letter or answer the email, they may be contacted by phone, mail or email to make sure that they have received the approach.		
Second contact	If potential subjects return the Reply Letter/reply to the email, or have called the investigator as first contact and are interested, the Investigator or delegated site personnel will contact the subjects by phone and give a short introduction to the investigation and go over the inclusion and exclusion criteria. If the subjects do not meet the inclusion criteria or meet the exclusion criteria, this will be registered at the Subject Screening Log.		
Subject Information Form	If subjects are eligible and interested in participating, then written information about the investigation (subject information) will be sent to the subjects to ensure that they are given the opportunity to read about the investigation before a possible informational visit, and for them to prepare any possible questions they may have. 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.		
First visit Information visit	If an eligible subject is interested in participating after the first contact, a visit will be arranged in a room reserved to ensure privacy and quiet surroundings at the investigators clinic/department. When arranging the visit, it will be ensured, that the subject has received the Information Form prior to the visit. The subjects will receive both written and verbal information about the possibility of bringing a companion to the informational visit and to any possible subsequent visits. See section 13 for information to be given to the subjects, as well as the informed consent process.		
Enrolment and inclusion visit (V0)	The subjects have the right to wait before deciding on participation. If/when the subject decides to participate, he/she will be asked to sign the relevant forms (see section 13). If a subject so desires, and it is certain that it is understood what the investigation entails, and the relevant forms have been signed the subjects are considered enrolled in the investigation.		

The coordinating clinical manager will have close contact to each site during the recruitment period. The principal investigator, or delegate, at each site will notify the clinical manager of all planned inclusion visits and whenever a subject is enrolled.

When either 48 1-piece or 2-piece users have been included, the inclusion of the respective group, will be paused, to aim for 48 1-piece users and 48 2-piece users to be included.

When the coordinating clinical manager is aware that 96 subjects have been included and randomised, the recruitment will stop. Subjects who have been informed of the investigation and are reflecting on their participation may be included within the first 24 hours hereafter.

[redacted]

Recruitment will occur through competitive recruitment in five countries: the Netherlands, Norway, UK, Italy and Germany. The number of countries is chosen to be sure that we can recruit enough subjects within the investigation timelines.
The recruitment period from first subject enrolled to last subject enrolled will be approximately six weeks.

6.3. Subject withdrawal/lost to follow up criteria

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

The investigator must withdraw a subject from the investigation due to:

- Noncompliance with the CIP impacting the scientific integrity of the investigation.
- If subject's safety and wellbeing is compromised by further participation.
- Pregnancy (see section 6.1.3 Pregnancy and breastfeeding)
- Compromise of exclusion criteria 1. or 2. regarding steroid, radio- og chemotherapy

6.3.1. Screening failures

Screening failures are considered subjects that have signed the informed consent form and been included based on in- and exclusion criteria, but not yet randomised.

Subjects that have signed the informed consent form but fails to comply with the in- and exclusion criteria are also considered screening failures.

Screening failures can be replaced by a new subject.

6.4. Point of enrolment

A subject is considered enrolled in the investigation when the written informed consent is obtained. The expected duration for each subject is described in section 4.1.

6.5. 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 delegate, 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, Medical Advisor or Data Safety and Monitoring board, 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 delegate at the site.

7. Procedures

7.1. Clinical investigation-related procedures

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

See section 7.2 Flow-chart for a more detailed overview of the clinical investigation-related procedures at visits, phone visits and at product/baseplate change.

7.1.1. Site visits

Visit 0 (Inclusion visit)
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 investigators clinic/department. When arranging the visit, it will be ensured, that the subject has received the Subject Information Form prior to the visit. The subjects will receive both written and verbal information to ensure that the subject understands what was read and explained and can freely agree to participate in the investigation. The subject will, beforehand, also be informed about the possibility of bringing a- companion to Visit 0 and to any possible subsequent visits. During the visit the principal Investigator, or delegate, will provide oral information about the investigation based on the Subject Information Form. The subject has the right to wait before deciding on participation.

If/when subjects decide to participate, they will be asked to sign the Informed Consent Signature Form. Hereafter, relevant female subjects will be asked to 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 allocated a subject number.

Visit 0 and visit 1 can be combined.

Test visits (V1, V2 and V3)
During test visit 1, the subject will be randomised to either treatment Arm A or Arm B and will be allocated a randomisation number. Hereafter the baseline questions will be completed by the Principal Investigator, or delegate. 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 delegate, will assess the skin and complete questionnaires about the subject's peristomal skin condition and ask the subject about stoma behaviour since last visit/call. The

subject will, at each test visit, complete questionnaires about e.g. skin condition, stoma behaviour, leakage and quality of life. Additionally, the principal investigator, or delegate, will take a photo of the peristomal skin , for assessment of changes in peristomal skin condition from Test visit 1 to Test visit 2, and from test visit 2 to test visit 3.

At test visit 2 and 3 the Principal Investigator, or delegate, will also complete questionnaires about changes in peristomal skin condition. The subject will also complete questionnaires about changes in peristomal skin conditions, feeling of security and handling of the product.

It must be ensured that the subject sits alone in a room reserved to ensure privacy and quiet surroundings and is in disturbed f when the completing the questionnaires at the visit.

7.1.2. Visit calls

At the visit calls (week 2, 4 8 and 10 after visit 1), the Principal Investigator, or delegate, calls the subject to follow-up since the last visit/call. The PI will ask about the product, the clinical trial app, peristomal skin condition and stoma behaviour.

7.1.3. Product change

Every time the subject changes the full product or baseplate (2-piece users) they will use the clinical trial app to complete a questionnaire about skin condition, reason for change, use of accessories and ballooning. In addition, they will be asked to take photos of the peristomal skin and the back side of the removed product (leakage).

7.1.4. Safety

Safety (adverse events, device deficiencies) will be assessed at all visits, planned and unplanned phone calls.

7.1.5. Follow-up after the investigation

Subjects who do not have an ongoing AE are not followed termination of the investigation. For ongoing AEs at investigation termination, please see section 14.4. All subjects are encouraged to contact the Principal Investigator, if they experience problems that they believe are related to their participation. This is to ensure that any device-related events are documented and to safeguard the subjects' health.

7.1.6. Interview

In this investigation eight-twelve subjects in UK might be interviewed to include some [redacted]

- [redacted]

[redacted] will be conducted as a telephone interview. The interviews, or relevant parts, will be tape recorded. It will not be possible to identify the subject from tape records. The subjects will be asked for consent, which include consent for the site personnel to forward the subjects contact information to the company performing the interview.

[redacted]

7.2. Flow-chart

Table 3 chart showing the connection between visits and assessments. [1] Investigator, or delegated personnel.

Assessment	Performed by	Inclusion visit (V0)	Visit 1 Test visit (V1)	Visit 2 Test visit (V2)	Visit 3 Test visit and Close-out (V3)	Visit call
Oral information	Investigator[1]	X				
Written informed consent	Subject	X				
Check of inclusion and exclusion criteria	Investigator[1]	X				
Pregnancy test (urine sample) – females only	Subject	X				
Subject number allocated	Investigator	X				
Randomisation	Investigator		X			
Registration of Baseline data	Investigator[1]		X			
Introduction to Clinical Trial App	Investigator[1]	X				
Assessment of subject wellbeing and compliance with CIP	Investigator[1]	X	X	X	X	X
Record change of product in Clinical Trial App, including photos and completion of questions related to change of product	Subject		X	X	X	
Photo of peristomal skin for assessment of changes in skin condition	Investigator		X	X	X	
Complete visit questions in eCRF	Investigator[1]		X	X	X	
Complete visit questions in Clinical Trial App	Subject		X	X	X	
Investigational product hand-out according to randomisation	Investigatior[1]		X	X		
Subjects trained in how to prepare skin for the Investigational product handed out, and how to use, handle, cut and store the product, according to IFU.	Investigatior[1]		X	X		
Hand-out remuneration and obtain signature	Investigatior[1]/subject		X	X	X	
Arrange dates for the next test visit and calls	Investigatior[1]	X	X	X		
Inform Clinical Manager about scheduled visits	Investigatior[1]	X	X	X		
Adverse events incl. supplementary information	Investigator[1]		X	X	X	X
Device Deficiencies	Investigator[1]		X	X	X	X
Concomitant medication	Investigator[1]	X	X	X	X	X

[redacted]

7.3. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in an electronic CRF (eCRF) or an application (Clinical trial App) in a provided phone for each subject.

Assessments completed by the principal Investigator, or delegate, will be recorded in the eCRF. Questions completed by the subject at visits or at every product (1pc) or baseplate change (2pc) will be recorded in the Clinical Trial App. All data completed in the Clinical Trial App will be uploaded directly to the data base when the phone is on a network.

CRFs will be completed by the subject, and/or by the principal investigator, or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log.

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

7.4. Concomitant treatment

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

Subjects are not allowed to use barrier cream or barrier film during the investigation.

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 chemotherapy is allowed for indications other than cancer

Steroid products on peristomal skin may interfere with the skin condition and use can make the skin more fragile to change of baseplates. Therefore, subjects are not allowed to use topical steroid treatment in the peristomal skin area e.g.

- 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.

8. Risk – benefit analysis

8.1. Risk-benefit analysis of the Coloplast investigational product

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 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.

[redacted]

To mitigate and reduce the risks, the users 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.

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

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

The test products contain a [redacted] 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 [redacted] 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 app at each change of product. The subjects are also asked to use a CE-marked competitor product for the comparator test period that may not be their preferred product on the market.

The participating subjects will contribute with important information for development of new stoma products, that may have less negative impact on the peristomal skin. 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 will be used including on-site, remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

9. Monitoring

The data collected throughout the investigation and the conduct of the investigation, will be monitored 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 details in the Monitoring Plan.

The monitoring will be conducted periodically at all sites by qualified designee personnel. The monitoring of this clinical investigation in Netherlands and Italy has be delegated by the sponsor to [redacted]
The investigator must be available for and agrees to cooperate with Coloplast Clinical Managers (CM) and/or CRO 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

[redacted]

- Periodic Monitoring visits
- Close Out visit

9.1. Periodic Monitoring visit(s)

Periodic Monitoring visit on site will be performed as soon as reasonable possible, after the site has enrolled the first subject in the investigation. This visit must be planned in order to up front minimise systematic errors done by site or subjects.

A monitoring visit on site will be performed after all subjects on site have completed the investigation. The CM/CRA shall have close contact to the Principal Investigators/sites during the conduct of the investigation, to ensure that any concerns, problems or recruitment challenges are solved with the site in a timely manner. If further monitoring visits on site or calls with site are required, this will be effectuated as needed.

Centralised monitoring reviewing data entered in the eCRF and the Subject's Clinical Trial App, will be performed by Coloplast CM throughout the conduct of the investigation.

The CRO CRA shall inform the sponsor about any problems relating to facilities, technical equipment or site personnel 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.

10. Source data verification

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

All documents and data related to the clinical investigation handled by site personnel, shall be produced and maintained in a way that assures reliability, integrity, control and traceability, and shall be appropriately stored to provide a complete history.

The Principal Investigator shall assure the accuracy, attribution, completeness, legibility and timeliness of the data reported to the sponsor in the eCRFs and in all required reports. All printed copies of electronic source documents shall be certified, as indicated by a dated signature by the investigational site personnel at the time the document is printed. Special requirements should be applied to the capture, review and retention of electronic source data, to ensure reliability, quality, integrity and traceability.

The data reported in the eCRFs 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, delegated site personnel 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.

11. Statistical considerations

11.1. Statistical design, method and analytical procedures

The primary objective will be evaluated by analysing the primary and secondary endpoints. These analyses are carried out by Medical Affairs, Coloplast A/S and are described in the following. The secondary objective regarding the [redacted] will be evaluated out by [redacted] and [redacted]

All baseline measurements, endpoints and other measurements (see Appendix 1 - Endpoints) will be summarized by descriptive statistics and/or listed. Endpoints and other measurements will be summarized by product, product type (1- or2-pc) and visit, if relevant. 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.

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

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

Definition of analysis populations
Intention to Treat (ITT), Safety and Per Protocol (PP) populations will be defined at a formal data review meeting just before database lock. As a minimum, the 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, and with valid information on at least one product with respect to either primary or secondary endpoints.

The PP population will be constituted by a subset of ITT subjects who fulfilled the inclusion/exclusion criteria and did not violate the protocol in a serious way

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.

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

Analysis of the primary endpoint
Max itching score within a week at steady state will be analysed by a mixed repeated measures model using individual week max scores (on a scale from 0-10) 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-pc), a fixed interaction between product and product type, a fixed period effect, an interaction between period and product, a random effect of subject and a random interaction effect of product and subject.

The model might be reduced by removing non-significant fixed effects, if relevant. The interaction between period and product allows for a possible carry-over effect. It is assumed that a possible carry-over effect is the

same for 1- and 2-pc users. If the interaction is significant, data from only the first test period will be analysed as a parallel arm study because the first period is free of carry-over effects and period will be excluded from the model.

All combinations of differences between the two products will be estimated for both 1- and 2- pc products. Furthermore, differences for same product between product types will be estimated (if the model is not reduced).

Analysis of the secondary endpoints

The endpoints regarding pain, burning, physical discomfort, ability to move around and the overall ability to stick the baseplate to the skin (on a scale from 0-10) will be analysed by the same model as the primary endpoint starting by calculating the max within a week at steady state.

[redacted]endpoints regarding bleeding (Y/N), experiencing any weeping or moisture (Y/N) and Ulcers or sores (Y/N) per baseplate change at steady state will be analysed by a repeated logistic regression model with the same effects included as for the primary endpoint.

The total DET 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. The endpoints regarding individual item scores (discoloration, erosion and tissue overgrowth) can be analysed by the same model, if relevant.

The discoloration area and intensity at steady state will be analysed by the same model as described for the primary endpoint. For these analyses the data from the individual skin photos are the observational unit.

The endpoints regarding frequency in the past 14 days by end of treatment (of itching, pain and burning) will be analysed similar to the analysis of total DET score. Instead of a mixed model, a generalized linear mixed model, namely a proportional odds model, will be applied for the analysis as the response is on a 5-point scale. Proc Glimmix will be applied for the analysis.

Analyses of exploratory endpoints

The leakage area and leakage diameter at steady state will be analyzed by the same model as the discoloration area and intensity described under secondary endpoints.

The median wear time will be analyzed by the same model as the total DET score. The median wear time per subject is based on data from the 3 last weeks in each period.

The three scores from the leakage scale questionnaire (emotional impact, usual/social activities, coping/control) as well as the total score and the sub-scores (discreetness, comfort, confidence and social life) from the quality of life questionnaire will be analyzed by the same model as the total DET score.

The endpoint regarding feeling of security as well as the 3 endpoints regarding handling will be analyzed by the same proportional odds model as described for the frequency of itching in the past 14 days by end of treatment.

The proportion of subejcts preferring test product will be compared with the proportion preferring the comparator by a test in the binomial distribution, testing the hypothesis that the proportions are equal.

Analyses of safety endpoints

Adverse events will be listed and summarized, if relevant.

11.2. Sample size

The itching score is given at each baseplate change and the max of these scores per week at steady state is the primary endpoint. The max score is only calculated if there are measurement for more than four days within a week. For each subject approximately three measurements will be available for each test period.

The sample size calculation is based on a simplified linear mixed model with only 1-pc users and no period effect (corresponding to the design from CP300). 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.

Based on data from CP300 it is assumed that the total standard deviation of the primary endpoint is 1.82 and that the total variation 1.82^2 is divided so that:

- a random effect of subject accounts for 68% of the total variation
- a random interaction effect of product and subject accounts for 0%
- and the residual accounts for 32% of the total variation

In table 1 the needed sample size is calculated by simulation for varying values of the true difference between comparator and test product regarding mean max itching score per week and for different values of the power to demonstrate that the difference is significantly different from 0.

Table 4: Subjects needed for comparing mean max itching score between two products

True difference	Reduction in mean if the mean for the comparator is 2.2 as for [redacted] in CP300	Power		
		0.8	0.85	0.9
0.6	27%	46	>46	>46
0.7	32%	35	40	45
0.8	36%	30	32	36

Based on the numbers in the table, 40 subjects should test each product to ensure a power of 85%, if the true difference between the comparator product and a test product is 0.7 (corresponding to a 32% reduction if the mean for the comparator is 2.2 as in CP300). This will be enough when comparing the two products. 1-pc and 2-pc users will be evaluated separately (in a combined model). As there are no previous data for 2-pc users the sample size calculations for 1-pc users is assumed to cover 2-pc users as well. To take a potential drop-out (20%) into account it is recommended to include a total of 48 1-pc and 48 2-pc users, resulting in a total of 96 subjects.

If a carry-over effect is present and therefore data from only the first period is analysed as a parallel arm trial 40 subjects (20 in each arm) will ensure a power of 82% if the true difference between the comparator product and the test product is 1.7. If there are no significant difference between 1- and 2-pc users, 80 subjects (40 in each arm) will ensure a power of 83% if the true difference between the comparator product and the test product is 1.2 (the difference in CP300 was estimated to 1.3).

The total number of 80 subjects is the required number of subjects for the [redacted]

11.3. Level of significance and power

A significance level of 5% will be applied. For a description of the power see section 11.2 above.

[redacted]

11.4. Pass/fail criteria

The purpose of the investigation is fulfilled if a significant difference in one of the skin endpoints is estimated.

11.5. Interim analysis

There is no planned interim analysis in this investigation that will affect the evaluation of the primary objective. To facilitate the evaluation of the secondary objective regarding evaluation of the [redacted] a data migration will be provided to the external partner [redacted] before DBL. The data migration will be based on data from all subjects having finalized visit 2. Any results of the analyses of data from [redacted] before DBL will be for the use of [redacted] only and not reported to Coloplast A/S.

11.6. Statistical reason for termination of investigation

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

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

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

12. Data collection and data management

12.1. Data Collection in the clinical investigation

Data will be collected through an electronic data capturing system on the 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 data management system is delivered by Medidata Solutions and is named Rave. Current version number is version 2018 2.2. The system is designed for electronic data capture, and it is 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. The system has full audit trail and electronic signature.

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 These data will be uploaded to the data base on a continuously basis. The electronic CRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up. 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 subject will receive a smartphone with the Clinical Trial App installed. The app is developed on behalf of Coloplast A/S by the app development company [redacted] This Clinical Trial App is used during the investigation every time the subject makes a product (1pc) or baseplate (2pc) change.

All data must be recorded in the eCRF during the visit or immediately after.

12.2. Database Management and Quality Control

The data management system has restricted role-based access control. The principal investigator or delegate must be trained in the system prior to getting access. The training is web-based and must be completed before

[redacted]

access to the investigation is granted. Training will be documented in the data management system. Only the principal investigator, or delegate, will be authorised to enter data in the eCRF,

The principal investigator can delegate tasks to his/her collaborators, however the roles and responsibilities as time period of involvement for each clinical site personnel must be documented on the delegation log as well as training received before getting involved with the clinical investigation must be documented in the training log.

The monitor, using his/her personal login information shall verify all critical data points against the source documents and issue electronic queries for the authorised clinical site personnel to respond, as defined in the monitoring plan.

The principal investigator, using his/her personal login information shall sign each case report form in the EDC system.

Automated, real time access to the data enable control on study compliance and safety assessments. Automated alerts (emails) are generated by the system to ensure full control and easier compliance to the clinical investigation plan.

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 released in the system as a query to 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 (site personnel, monitor, sponsor, data manager) access to the system is tracked, so that all data operations can be followed for monitoring and verification.

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 data management system.

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

Data management and the final statistical analyses of all measurements described in this protocol are carried out by the, Medical Affairs, Coloplast A/S. The evaluation of the [redacted] is carried out by [redacted] according to the SAP.

12.4. Data retention

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

13. Amendments to the CIP

No changes in the clinical investigation procedures shall be affected without mutual agreement of the principal investigator and the sponsor. The agreement of the changes must be documented by signing the corresponding clinical investigation plan amendments. All changes must be registered in the Change Log with a rationale.

All changes require notification to the EC and the CA (when appropriate). Substantial changes may require approval from the EC and the CA prior to implementation.

14. Deviations from Clinical Investigation Plan

Every effort should be made to avoid deviations from the clinical investigation plan during the conduct of the investigation. The Investigator is not allowed to deviate from the CIP unless under emergency circumstances and to protect the rights, safety and well-being of the subject(s). Deviations must be reported to sponsor and deviations affecting the scientific aspect of the investigation or the safety of the subject (violation) are reported to the EC and regulatory authorities by sponsor if required by national regulations.

For reporting purposes, the sponsor classifies study deviations as major and minor:

Major deviation: Any deviation that may either have an impact on the rights, safety and well-being of the subjects or the scientific outcome of the clinical investigation.

Minor deviation: Any deviation that has no impact on the rights, safety and well-being of the subject or that may impair the scientific outcome of the clinical investigation.

The Investigator should inform the CM/CRA of any deviation, and the implications of each deviation must be reviewed and discussed. If the deviation affect the subject, discussion for a decision on the further participation of the subject should be completed. Any deviation must be documented, stating the reasons, date, actions taken, and the impact for the subject and/or investigation. This documentation must be kept either in the Deviation Log in the Investigator Site File or in the Deviation CRF form, depending on the deviation's relation to either the data collected in the CRF or all other case of any deviations on site.
Deviations occurring outside of the investigation site, by vendors will be documented by the Sponsor.

15. Accountability of investigational products

All access to the investigational products (non-CE marked investigational product and CE marked comparator investigational products) used in the clinical investigation is controlled by storage procedures and accountability logs as described below. The Coloplast investigational product must only be used in this clinical investigation and only according to the CIP.

Sponsor keeps an accountability log that states the physical location of all investigational products from shipment of investigational products to the investigational sites until return of or disposal.

The PI or delegate keeps records documenting the receipt, use and return and disposal of the investigational products, 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

[redacted]

16. Statement of compliance

The clinical investigation is conducted in accordance to:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Brazil, October 2013.
- MDD 93/42/EEC as amended by Directive 2007/47/EC (commonly known as the Medical Device Directive).
- 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.

16.1. 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.

16.2. Data protection

As part of the investigation Coloplast A/S, Holtedam 1, 3050 Humlebaek, Denmark ("Coloplast") will collect and process the personal information that the subjects provide for the investigation ("personal data"). This includes identification and contact information (which will be anonymised) as well as information about product usage experience and health. Coloplast will only process personal data:

1. To conduct the investigation and carry out related research based on the subjects consent (primary use), cf. article 9(2)(a) of the EU General Data Protection Regulation (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 your personal data, cf. article 9(2)(a) of GDPR –carry out research outside the clinical protocol to improve Coloplast's products and services, and for use in education.

Part of Coloplast's processing is carried out on third-party platforms (clinical trial databases) and certain third parties are assisting Coloplast in the processing (e.g. the investigator). Such cases will imply a transfer of personal data to the third parties, but solely for the specified purposes and with the third parties acting on instruction from Coloplast. Data may be collected and processed across the Coloplast network, which may entail processing of personal data outside the European Economic Area. In such cases, an adequate level of protection will be ensured by the third parties being subject to the standard contractual clauses on data protection adopted by the EU or to an EU-approved certification mechanism on data protection. For further information about this please consult Coloplast's data protection officer (details below).

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. Personal data will be deleted at the end of the mandatory retention

period. If the subject wish to learn more about how Coloplast processes personal data, they can visit www.coloplast.com/global/privacy-notice.

If the subject have questions or queries regarding Coloplast's handling of personal information, they must contact Coloplast's Data Protection Officer at [redacted] Complaints related to Coloplast's handling of personal information may similarly be sent to the Data Protection Officer, and subjects are 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).

Subjects can write to [redacted] at any time to request:

1. Access to their data
2. Correction of errors in their data or to erase their data
3. Limit what can be done with their data
4. To receive their data in machine-readable format (data portability).
5. Withdrawal of consents they have given Coloplast to process their data

16.3. Financial conditions

16.3.1. Investigator payment

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

16.3.2. Subject compensation

The subject will receive payment for their participation in the investigation. They will be paid cash in local currency based on the below numbers. The compensation in taxable, according to national regulations. In addition, the subjects will be compensated for transportation to the site. The

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

16.3.3. 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. 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 principal investigator, or delegate 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. 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 principal investigator, or delegate responsible for conducting the informed consent process. A copy will be provided to the subject.

If new information is to be given during the investigation, sponsor will inform the principal investigators, and the new information is given to the subjects by the principal 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. Clinical manager is responsible for writing the information and providing it to principal 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.

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.

18.2.1. Anticipated device effects

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

Example: A 1pc. stoma bag is badly adhered to the baseplate and induce leakage of output.

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

18.6.1. Investigator's reporting responsibilities

- PI, or delegate, 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 events, the relationship to the Investigation product and the intensity of the event shall be described whether the event is considered

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

or the event is considered

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

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

Please report to:

[redacted]

18.6.2. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported to national regulatory authorities and ethics committees, as applicable, immediately, but no later than seven calendar days following the date of awareness by sponsor.

- All serious adverse events.

[redacted]

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

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

It is the responsibility of sponsor to inform all investigators in writing within ten 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).

18.6.2.1 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.

18.6.2.2 Data Safety and Monitoring Board

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 as well as the data analyses, including statistical results and conclusions.

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

Coloplast, sponsor, is referring to the internal document 'Clinical Publication Policy' that will be available for internal and external persons involved in the publication process.

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

22. Appendix

22.1. Appendix 1 - Endpoints

The column "Description of endpoints" includes endpoints where the corresponding analysis is described in the statistical analysis section. The column "Measurement" includes measurements that will be summarized and/or listed. The column "Derived from" describes the questions in the eCRF/APP or the method used as basis for the endpoint or measurement. The three last weeks in each test period is in the table referred to as "steady state".

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
Primary	Itching	*1.* Max itching score within a week at steady state		The individual itching score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
Secondary			Max itching score per baseplate change (0-10) at steady state Frequency of itching per baseplate change at steady state	How much of the time have you experienced any **itching** around your stoma since you last changed your product? *(tick one box only)* • None of the time • A little of the time • Some of the time • A lot of the time • All of the time Please rate how itchy the skin around your stoma has been <u>at its worst</u> since you last changed your product *(tick one box only)* (Scale from 1-10, very mild itch – worst itch possible)	**Skin condition** [redacted]	**Subject**					**X**
		2. Frequency of itching in		How often have you experienced itchy skin around your stoma in the past 14 days?	**Skin condition (Visit CRF)**	**Subject**		**X**	**X**		

Type of endpoint	Group of end-point	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		the past 14 days by end of treatment		• None of the time • A little of the time • Some of the time • A lot of the time • All of the time							
	Pain	3. Max pain score within a week at steady state		The individual pain score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
			Max pain score per baseplate change (0-10) at steady state Frequency of pain per baseplate change at steady state	How much of the time have you experienced any pain around your stoma since you last changed your product? *(tick one box only)* • None of the time • A little of the time • Some of the time • A lot of the time All of the time Please rate how **painful** the skin around your stoma has been <u>at its worst</u> since you last changed your product *(tick one box only)* (Scale from 1-10, very mild pain – worst pain possible)	**Skin condition** [redacted]	**Subject**					**X**
		4. Frequency of pain in the past 14		How often have you experi-enced any pain in the skin around the stoma in the past 14 days?	**Skin condition**	**Subject**		**X**	**X**		

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		days by end of treatment		• None of the time • A little of the time • Some of the time • A lot of the time • All of the time							
	Burning	5. Max burning score within a week at steady state		The individual burning score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
			Max burning score per baseplate change (0-10) at steady state Frequency of burning per baseplate change at steady state	How much of the time have you experienced any burning feelings from the skin around your stoma since you last changed your product? *(tick one box only)* • None of the time • A little of the time • Some of the time • A lot of the time • All of the time Please rate any burning feelings from the skin around your stoma <u>at its worst</u> since you last changed your product *(tick one box only)* (Scale from 1-10, very mild burning – worst burning possible)	**Skin condition** [redacted]	**Subject**					**X**

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		6. Frequency of burning in the past 14 days by end of treatment		How often have you experienced burning feelings in the skin around your stoma in the past 14 days? • None of the time • A little of the time • Some of the time • A lot of the time • All of the time	**Skin condition (Visit CRF)**	**Subject**		**X**	**X**		
	Bleeding/ Weeping or moist skin/ Ulcers or sores (DET score also includes an endpoint in this category)	Bleeding (Experiencing/Not experiencing) 7. per baseplate change at steady state Weeping or moist skin (Experiencing/Not experiencing) 8. per baseplate change at steady state Ulcers or sores (Experiencing/Not experiencing)		- Do you experience any **bleeding from the skin** around your stoma **right now** when changing your product? *(tick one box only)* (Experiencing/Not experiencing) - 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) - Are you experiencing any **ulcers or sores** around your stoma **right now** when	**Skin condition** [redacted]	**Subject**					**X**

[redacted]

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		9. per baseplate change at steady state		changing your product? *(tick one box only)* (Experiencing/Not experiencing)							
	Overall physical discomfort	10. Max overall physical discomfort score within a week at steady state		The individual **overall physical discomfort** score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
			Max overall physical discomfort score per baseplate change (0-10) at steady state	How would you rate your **overall physical discomfort** from skin around your stoma since you last changed your product? (tick one box only) (11-point scale from No discomfort to A lot of discomfort)	**Skin condition** [redacted]	**Subject**					**X**
	Overall ability to move around	11. Max overall ability to move around score within a week at steady state		The individual **overall ability to move around** score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
			Max overall ability to move around score per baseplate change (0-10) at steady state	How much have skin complications around your stoma caused you difficulty in your **overall ability to move around** since you last changed your product? For example,	**Skin condition** [redacted]	**Subject**					**X**

Type of endpoint	Group of end-point	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
				bending or walking (tick one box only)							
	Overall ability to stick the stoma bag adhesive to your skin	12. Max overall ability to stick the stoma bag adhesive to your skin score within a week at steady state		The individual **Overall ability to move around** score per baseplate on a scale from 0-10 (see question below)	**Skin condition** [redacted]	**Sponsor**					**X**
			Max overall ability to stick the stoma bag adhesive to your skin change (0-10) score per baseplate at steady state	How much have skin complications around your stoma caused you difficulty **in your overall ability to stick the stoma bag adhesive to your skin** since you last changed your product? (tick one box only)	**Skin condition** [redacted]	**Subject**					**X**
	Discoloration (DET score also includes a discoloration endpoint	13. Discoloration area score (cm^2) per baseplate change at steady state		Based on discoloration area in different zones close to the stoma estimated by [redacted] from photos of the skin	**Skin condition (photos of skin)**	**Sponsor, from photos taken by subject**					**X**
	Intensity	14. Intensity score (cm^2) in the inner zone per baseplate change at steady state		Based on area with a given intensity estimated by [redacted] from photos of the skin	**Skin condition (photos of skin)**	**Sponsor, from photos taken by subjects**					**X**

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		15. Intensity score (cm^2) in the outer zone per baseplate change at steady state									
	[redacted]	16. [redacted]		[redacted]	[redacted]	**Sponsor**					
	DET score	17. Total DET score by end of treatment 18. Discoloration item score by end of treatment 19. Erosion item score by end of treatment 20. Tissue overgrowth item score by	-	- Area of discoloration (Score 0-3) - Severity of discoloration (Score 1-2) - Area of erosion (Score 0-3) - Severity of erosion (Score 1-2) - Area of tissue overgrowth (Score 0-3) - Severity of tissue overgrowth (Score 1-2)	**Skin condition (DET score) from skin photos[3]**	**Based on app photos** **Sponsor/HCP assessment from visit photos**	**X**	**X**	**X**		

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		end of treatment									
Explorative endpoints			Is there discoloration of peristomal skin with complications? (Yes/No) by end of treatment	Is there discoloration of peristomal skin **with complications** (pain, shiny, indurated, hot, itching, burning)? (Yes/no)	**Skin condition (DET score)**	**Investigator (subject)**	**X**	**X**	**X**		
			Is there damage to the lower layers of the skin with complications? (Yes/no) by end of treatment	Is there damage to the lower layers of the skin **with complications** (moisture, bleeding or ulceration)? (Yes/no)	**Skin condition (DET score)**	**Investigator**	**X**	**X**	**X**		
			Is there raised tissue above skin level with complications? (Yes/no) by end of treatment	Is there raised tissue above skin level **with complications** (bleeding, pain or moisture)? (Yes/no)	**Skin condition (DET score)**	**Investigator (Subject)**	**X**	**X**	**X**		
	Stoma behaviour		Stoma behave differently from normal? (Yes/No) by end of treatment	Did your stoma behave differently from normal since your last visit/call? (Yes/No) -If yes, please specify	**Visit CRF**	**Subject**	**X**	**X**	**X**	**X**	
	Feeling of security	**21.** Feeling of security while wearing the product (5-point scale) by end of treatment		How was the feeling of security while wearing the product? (5-point scale from Very poor to Very good)	**Visit CRF**	**Subject**		**X**	**X**		
	Handling	**22.** Cutting the baseplate (5-point scale) by		How did you find cutting the baseplate? (5-point scale from very difficult to very easy)	**Visit CRF**	**Subject**		**X**	**X**		

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		end of treatment									
		23. Applying the baseplate (5-point scale) by end of treatment		How did you find applying the baseplate? (5-point scale from very difficult to very easy)	**Visit CRF**	**Subject**		**X**	**X**		
		24. Removing the baseplate? (5-point scale) by end of treatment		How did you find removing the baseplate? (5-point scale from very difficult to very easy)	**Visit CRF**	**Subject**		**X**	**X**		
	Leakage	25. Emotional impact score by end of treatment 26. Usual/social activities score by end of treatment 27. Coping/control score by end of treatment		On a scale from 0-100 calculated based on the questions from the Leakage scale questionnaire	**Leakage scale questionnaire**	**Subject fills in the questions and the sponsor calculates the score**	**X**	**X**	**X**		
		28. Leakage distance (cm) by baseplate		Estimated by [redacted] from photos of the baseplate	**Leakage (photo of baseplate)**	**Sponsor, from photos taken by subject**					**X**

[redacted]

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
		change at steady state									
		29. Leakage area (cm^2) by baseplate change at steady state		Estimated by [redacted] from photos of the baseplate	**Leakage (photos of baseplate)**	**Sponsor, from photos taken by subjects**					**X**
	Quality of life	30. Total HQoL score (0-92) by end of treatment 31. Discreetness score (0-24) by end of treatment 32. Comfort score (0-24) by end of treatment 33. Confidence (0-24) score by end of treatment 34. Social life (0-20) score by end of treatment		**C**alculated based on the questions from the Quality of life questionnaire	**Quality of life questionnaire (Ostomy-Q)**	**Subject fills in the questions and the sponsor calculates the score**	**X**	**X**	**X**		
	Preference	35. Proportion of preference of test product or SC?		Which product do you prefer? (The product from the first test period, the product from the second test period?)	**Visit CRF**	**Subject**			**X**		

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
			Reason for preferring test product or SC	Why do you prefer this product over the other? - Less leakage - Better feeling of security - Better comfort - Better discretion - Less pancaking - Less ballooning - Better skin condition - Better ability to fit and follow the body - Other reason? *(You may tick more than one box)*	**Visit CRF**	**Subject**			**X**		
			Proportion of preference of test product, SC or own product?	**Preference** Which product do you prefer? (Your own product, The product from the first test period, the product from the second test period?)	**Visit CRF**	**Subject**			**X**		
			Reason for preferring test product, SC or own product	**Preference** Why do you prefer this product over the other? - Less leakage - Better feeling of security - Better comfort - Better discretion - Less pancaking - Less ballooning - Better skin condition - Better ability to fit and follow the body - Other reason?	**Visit CRF**	**Subject**			**X**		

Type of endpoint	Group of end-point	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
				(You may tick more than one box)							
	Reason for change		Reason for change by baseplate change at steady state	What was the main reason for changing the products? (14 choices + other text) - I followed my usual changing pattern - I thought it would be nice with a clean product - In preparation of an activity (i.e. going out, doing sports, travelling) - The entire baseplate had become detached - The outer edge of the baseplate had become detached - The centre of the baseplate had become detached - I was afraid the baseplate would become detached - The area around the stoma was itching - The area around the stoma was painful - There was leakage underneath **and** outside the baseplate - There was leakage underneath the baseplate (but not outside the baseplate)	**App**	**Subject**					**X**

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
				- The bag was full of air (ballooning) - There was vacuum in the bag (pancaking) - Due to test visit in the investigation - Other reason (text)							
			Was there leakage outside the baseplate? (Yes/no) by baseplate change at steady state	Was there leakage outside the baseplate (i.e. soiling the clothes)? (Yes/no)	**APP**	**Subject**					**X**
	Use of accessories		Accessories used? by baseplate change at steady state	Which stoma accessories did you use? - Adhesive remover - Paste - Rings - Wipes - Stoma tape - Stoma belt - Hernia belt - Stoma powder - Barrier lotion/crème/spray/wipes - Cleansing wipes/cleansing spray - Odour remover - Other accessories (text) *(You may tick more than one box)*	**APP**	**Subject**					**X**

[redacted]

Type of endpoint	Group of endpoint	Description of endpoint	Measurement	Derived from	Origen	Assessed by	V1	V2	V3	Calls	Product change
	Ballooning		Experience ballooning? (Yes/No) by each baseplate change at steady state	Did you experience the bag becoming overfilled with air during use (ballooning)? (Yes/No) If yes, how much did your bag become overfilled? (Not at all to very much)		**Subject**					**X**
	Wear time	36. Median wear time (hours) by treatment at steady state		The median wear time is calculated by summary statistics of the individual wear times of each baseplate	**Sponsor calculates wear time based on photos taken by the Subject**	**Sponsor**					**X**
Safety endpoints	**Adverse events**				**CRF**	**Investigator**	**X**	**X**	**X**	**X**	
	Device deficiencies				**CRF**	**Investigator**	**X**	**X**	**X**	**X**	
Not an endpoint	**Concomitant medication**				**CRF**	**Investigator**	**X**	**X**	**X**	**X**	

[redacted]

[redacted]

22.2. Appendix 2 – Leakage scale questionnaire

Emotional impact

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

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

Usual and Social activities

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

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

Coping and in control

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

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

22.3. Appendix 3 - Quality of life questionnaire

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

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

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

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

22.4. Appendix 4 – Baseline data

Baseline data – registered at the inclusion visit (V1) by Principal Investigator, or a delegate.

- Date of Informed Consent (date)
- Date of visit (date)
- Check of inclusion criteria
- Check of exclusion criteria
- Subject number (number - *automatically generated in eCRF*)
- Randomisation number (number - *automatically generated in eCRF*)
- Name/type of randomised product (list of investigational products)

Demographic

- Date of birth (date)
- Gender (male/female)
- Height (number - cm)
- Weight (number – kg)

Stoma

- 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)
- Size of the stoma (diameter on widest place and height)
- Shape of the stoma/intestine (round/oval/irregular)

Current product

- What is your Current product (brand, product name, item number, size, 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, stoma belt, Hernia belt, Stoma powder, Barrier lotion, barrier cream, barrier spray or barrier wipes, Cleansing wipes/cleansing spray, Odour remover, Other accessories)
  - If 'other accessories', please specify
- On average, how often do you normally change your product (1pc)/baseplate (2pc)? (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)

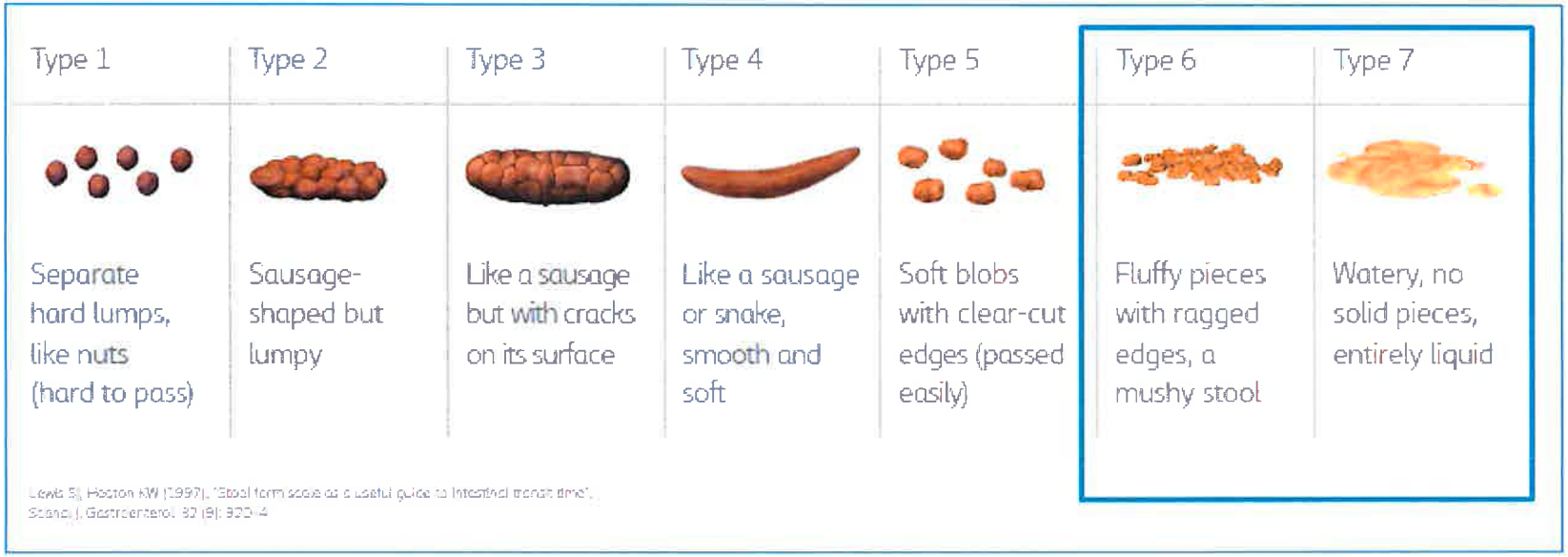
Peristomal skin area

- How often do you experience peristomal skin complications (itching, burning, red or discoloured skin, pain, bleeding, moist or broken skin)?)? (Daily, Every 2-3 days, every 4-6 days, Once a week, Once every second week, More rarely)
- Which peristomal skin complication/symptom do you experience most often? (itching, burning, red/discoloured skin, pain, bleeding, moist or broken skin)
- Body profile with body check tool
- How many times in the last year have you had a peristomal skin complication, where you had to seek consultation and/or treatment from a health care professional?

Leakage/output

- What is the frequency of your output? (All the time (continuous)/with regular intervals/with irregular intervals)
- Bristol scale score
- Do you experience ballooning (air in the bag)? (Yes/no)

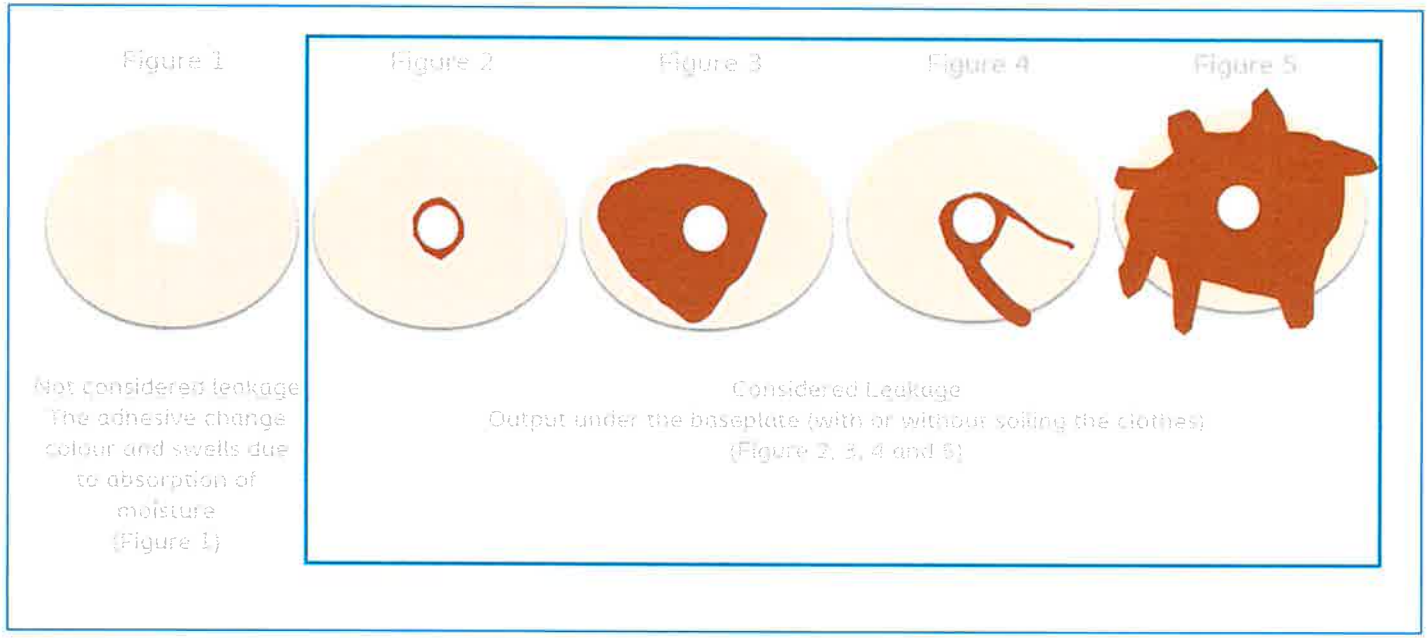
22.5. Appendix 5 - Bristol scale



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

[redacted]

22.6. Appendix 6 – Classification of leakage



[redacted]

[redacted]

Approved	[redacted] 02-Sep-2019 11:08:27 GMT+0000
Approved	[redacted] 02-Sep-2019 11:42:24 GMT+0000

[redacted]

[redacted]