Clinical Investigation Plan

CP340 SUN-Study

Investigation of patient benefits with a new supporting ostomy product and support service in patients with a newly stoma formation.

October 2021- October 2022

CHANGE LOG

VERSION NUMBER	ISSUED BY *(INITIALS)*	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	First approved version
2.0	[redacted]	Inclusion criteria "Has some, high or very high worry of leakage. Only applicable for subjects more than 3 months post-surgery" removed
3.0	[redacted]	Appendix 8+9 Visit dates corrected. Visit 2 corrected from week 6 to week 4 and visit 3 from week 10 to week 8. C.1 skin measurement follow visits. "X" moved to visit 2 week 4 and visit 3 week 8. Minor editorial changes
4.0	[redacted]	Fig 4 "App data flow high level" damaged during approval. Fig 4 restored
5.0	[redacted]	P.12 Heylo™ app software version have been updated from iOS 1.9.2.xxxx and Android 1.9.2.xxxx to iOS 2.2.0.xxxx and Android 2.2.0.xxxx. P58+P59 editorial change. Two X's moved from week 6 to week 4 (Visit 2) and two X's moved from week 10 to week 8 (visit 3)
6.0	[redacted]	Exclusion criteria 4. "Enrolled in another current research study or have previously participated in this investigation is changed to "Enrolled in another current ostomy device study or have previously participated in this investigation. Co-enrolment must be agreed with sponsor".

Approval date of version 6.0: 21. February 2022
NCT05135754

SYNOPSIS OF THE CLINICAL INVESTIGATION

The aim of the study is to investigate patient benefits associated with the utilisation of a new supporting ostomy product, when delivered together with an online support service.

Test products and comparator

- Skin adhesive Sensor Layer
- Blue tooth Transmitter which is connected to the Sensor Layer.
- A mobile phone Application (App) - This is installed on subject's smartphone and communicates the sensor status to the subject.
- Charger to the transmitter.
- Cable to the charger.
- Coloplast Charter Support Service
    - Coloplast Care service
    - Leakage service
    - Technical support

No comparator is used is this study.

Intended use:

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

Objective(s)

Primary objective
Is to investigate the incidence of stoma effluent leakage outside the baseplate when using the Test Product.

Secondary objectives

- To evaluate patient stoma self-management
- To evaluate health and leakage related quality of life
- To Assess patients' evaluation of the Test Product, including preference, interoperability and ease of use

Design of the investigation

The investigation is a multi-centered, open labelled, single arm case study, with an expected duration of the study of 12 weeks +/- 2 weeks.

Subjects are asked to fill in surveys at baseline and after 4, 6, 8, 10 and 12 weeks of test product use.

Primary endpoint and secondary endpoint(s)

Primary endpoint:

- Number of times with stoma effluent leakage outside the baseplate (e.g. onto clothes or bedsheets) within the last 2 weeks

Secondary endpoints:

- Patient Self-management (Patient Activation Measure (PAM)):
    - PAM score (0-100)
- Leakage related QoL (OLI):
    - Emotional impact score (0-100)
    - Usual/social activities score (0-100)
    - Coping/Control score (0-100)
- Health Related Quality of Life (EQ5D-5L):
    - EQ-5D-5L – index score (UK)
    - EQ-5D-5L – VAS score

Exploratory endpoints

- Skin condition measured by Decision Tree Score (0-3) based on Peristomal Skin Health (OST 2.0)
- Quality of Life WHO5 score (0-100) based on Mental wellbeing (WHO5)
- Worry about leakage (5-point scale)
- Feeling of security (5-point scale)
- Technical assurance/interoperability measured by system reliability, notification frequency and stability (all measures on 5-point scales)
- Usability and self-management evaluated through System Usability Score (0-100) and confidence measures (5-poins scales)
- Preference, recommendation and future use (5-point scales)
- Adverse events

Population/subjects

The investigation aims to include minimum 60 and maximum 90 subjects with ileostomy or colostomy with liquid/mushy output within a 6-month recruitment period. All subjects should have had their stoma formation within 9 months prior to inclusion and minimum 30 subjects are planned to be enrolled within the first 3 months after surgery.

Inclusion criteria:

1. Have provide written informed consent.
2. Be at least 18 years of age and have full capacity.
3. Have had their stoma for less than 9 months.
4. Have intact skin on the peristomal area (assessed by investigator)
5. Be able to use one of the five test products (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm)
6. Ileo- or colostomists with liquid and/or mushy output (Bristol scale type 5-7), see Appendix 1.
7. Is willing to refrain from use of paste and protective sheets.
8. Have a smartphone applicable for the Heylo™ app.
9. Have been self-managing stoma appliance for at least 14 days.
10. Are able to follow study procedures for 3 months (assessed by investigator)
11. Are willing to receive their ostomy products through Coloplast Charter for the duration of the study.

Exclusion criteria

1. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment.
2. Is breastfeeding.
3. Is pregnant based on urine pregnancy test.
4. Enrolled in another current ostomy device study or have previously participated in this investigation. Co-enrolment must be agreed with sponsor.
5. Has known hypersensitivity towards any of the products used in the investigation.
6. Is using/have a pacemaker.
7. Has a complicated stoma at baseline (dehiscence/prolapse/hernia)
8. Has limited life expectancy or receive palliative care.
9. Has stage 4 cancer.
10. Having more than one stoma synchronously
11. Having ongoing non-healed abdominal wounds
12. Reoperation / stoma reversal planned during the study period.

Investigational approval

The investigation will be approved by the Research Ethics Committee (REC) before the investigation can be initiated.

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 18.2
AE	Adverse Event	See section 18.1
ASADE	Anticipated Serious Adverse Device Effect	See section 18.4.2
CIP	Clinical Investigation Plan	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection
CM	Clinical Manager	
DQF	Data Query Forms	A DQF is a query specifically used in clinical research. The DQF is the primary data query tool from the sponsor to clarify discrepancies and ask the investigator for clarification. The DQF is part of the data validation process in a clinical investigation.
DD	Device deficiency	
EC	Ethics Committee	
IFU	Instruction For Use	
ITT	Intention to Treat	
PI	Principal Investigator	Qualified person responsible for conducting the clinical investigation at an investigation site. If the clinical investigation is conducted by a team of individuals at an investigation site, the PI is the responsible leader of the team. Whether this is the responsibility of an individual or an institution can depend on national regulations.
PP	Per Protocol	
SADE	Serious Adverse Device Effect	See section 18.4.1
SAE	Serious Adverse Event	See section 18.4
USADE	Unanticipated Serious Adverse Device Effect	See section 18.4.3

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1. List of personnel involved in the Investigation.

1.1. Sponsor representatives

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

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

1.2. Site Personnel

CHIEF INVESTIGATOR – SITE 1
[redacted]

This clinical investigation involves up to 10 sites in United Kingdom.

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

2. Rational/justification for conducting the clinical investigation

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

To overcome this, Coloplast has developed a new supporting ostomy product called Heylo™, which has an adhesive sensor layer that should be placed underneath the baseplate. The sensor layer consists of an electronic sensor system that continuously detects moisture and output leakage underneath the baseplate. A transmitter connected to the sensor layer continuously evaluates the incoming information and sends a status to a smartphone software application, which based on a predefined flow decides which information to deliver to the user about the baseplate status.

The overall aim of the study is to investigate the health impact of the new supporting ostomy product, when delivered together with a support service.

[redacted]

[redacted]

A clinical study CP321 has been planned and initiated including 25 subjects in Denmark, to confirm technical readiness with Android and iOS software and will be concluded upon before initiation of present study.

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

3.1. Objective (s)

Primary objective

Is to investigate the number of incidents of leakage of stoma effluent outside the baseplate when using the Test Product.

Secondary objectives

- To evaluate patient stoma self-management
- To evaluate health and leakage related quality of life.
- To Assess patients' evaluation of the Test Product, including preference, interoperability and ease of use.

3.2. Hypotheses

The study will explore if the Test Product leads to a significant decrease in incidents of leakage outside the baseplate compared to the period before entering the study and thereby possibly lead to secondary benefits such as improved feeling of leakage control, confidence, and security. Moreover, the Test Product may assist patients in managing their stoma and better understand general health aspects related to their condition, such as prevention of peristomal skin complications.

4. Investigational device and comparator(s)

The Test Product consist of 1) a physical product called Heylo™ and 2) Coloplast Charter Support Service.

The test product is used in combination with the ostomy baseplates usually used by the subject. Subjects will be supplied with a sufficient number of Heylo™ sensor layers to support their normal change routine.

4.1. Description of Test Product - Heylo™ system

The Heylo™ investigational device consists of the following:

- Adhesive patch - sensor layer (single use)
- Transmitter (re-use), to be connected to the sensor layer.
- Heylo™ app (installed on subject's own smartphones). The app is communicating sensor status to the subject.
- Charger to the transmitter incl. core

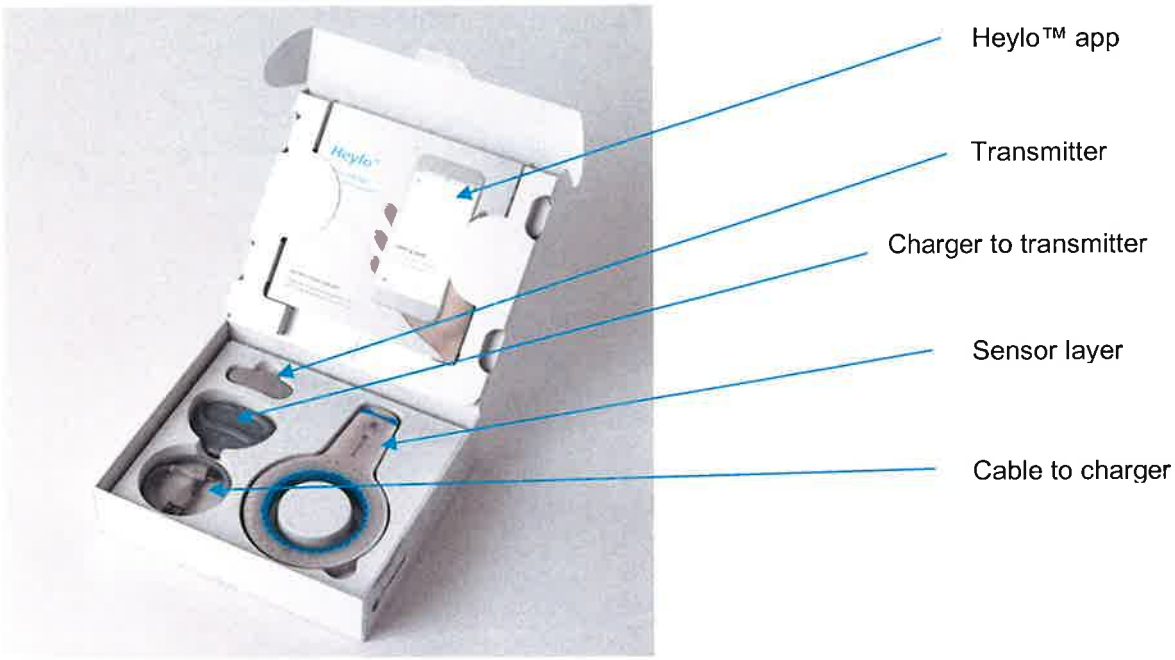


Figure 1: Investigational device - Heylo™

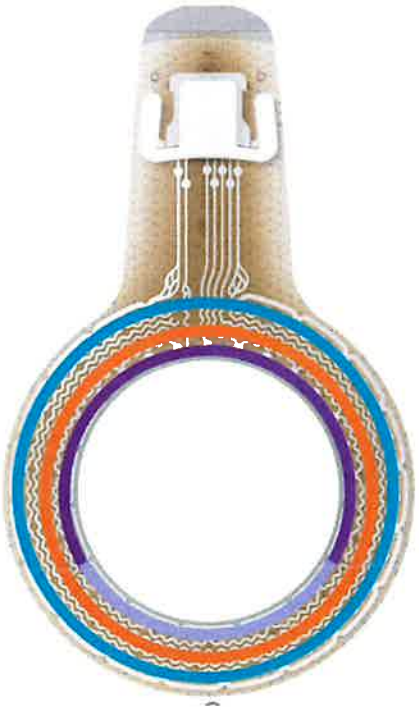


Figure 2 Sensor layer

The colours on the sensor layer are only illustrative and illustrate the different sensor elements.

- Turquoise: Outer leakage sensor. Detecting leak close to rim of baseplate
- Orange: Wear sensor. Detecting moisture absorbed by the adhesive material
- Purple: 3 inner leakage sensors. Detecting leak closest to stoma

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

Figure 3 Sensor layer appliance

Figure 4 App data flow high level

4.2. Description of Test Product - Coloplast Charter Support Service

Coloplast Charter Support Service is a call support service, consisting of 3 elements:

1. Coloplast Charter service
2. Leakage service
3. Technical support

Coloplast Charter Service

The existing Coloplast Charter Service offers support on products and routines and helps ostomates with product order and delivery.

Leakage service
If subjects have leakage issues, they have the possibility to call Coloplast Charter for Leakage support, and/or Coloplast Charter may reach out to the subject if subject is struggling with leakage (observed from Heylo app leakage data in cloud). In case subjects have questions related to how to change appliance or how to use/interpret the information provided by the Heylo™ app, subjects can also call Coloplast Charter Support through the Heylo™ app (number is provided in the app).

Technical support
If subjects have technical issues, they have the possibility to call Coloplast Charter for technical support, and/or Coloplast Charter may reach out to the subject if subject is struggling with technical issues (e.g. technical failure screens delivered to users, and system does not seem to get back running again).

4.3. Manufacturing

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

4.4. Identification and traceability of the device

The CE marked physical Test Product will be identified as Heylo™.

- Adhesive patch - sensor layer ID
  - ø40: 1921008000
  - ø50: 1921108000
  - ø60: 1921208000
  - ø70: 1921308000
  - ø80: 1921408000
- Transmitter ID 23323073
- Heylo™ app software version
  - iOS 2.2.0.xxxx
  - Android 2.2.0.xxxx
- Charger to the transmitter ID 23323072
- Charger cable ID: 23325128

4.5. Intended use of the device in the clinical investigation

Intended purpose of device:
The Heylo™ is intended to be used together with an ostomy baseplate and bag, to detect and notify user of the occurrence of output leakage under an ostomy baseplate.

Intended medical indication(s):
The product is indicated for users with an ostomy, mainly Ileostomy and colostomy with liquid output. The product is to be used on intact skin.

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

Application:
In the Instruction for Use (IFU), application, few warnings, cautions and pre-caution of how to use Heylo™ are given. See IFU [5+6]

4.6. Intended population for the device

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

4.7. Handling of the investigational device

The handling of Heylo™ is described in details in the Instruction for Use (IFU), which is included in all boxes with test products. Storage conditions are also stated in the IFU.

All Investigators / investigator representatives will receive training by sponsor / investigator in the handling and correct use of the test products. The Investigator/investigator representative will train the subjects in the correct use of the Test Products.

4.8. Total number of devices intended for the clinical investigation

Each subject will be supplied with Heylo™ app and study supplies as described below:

- 1 charger
- 1 charging cable
- 1 charging adapter
- Two transmitters
- Sensor layers to support a daily change pattern + sufficient extra sensor layers

4.9. Description of the comparator product(s)

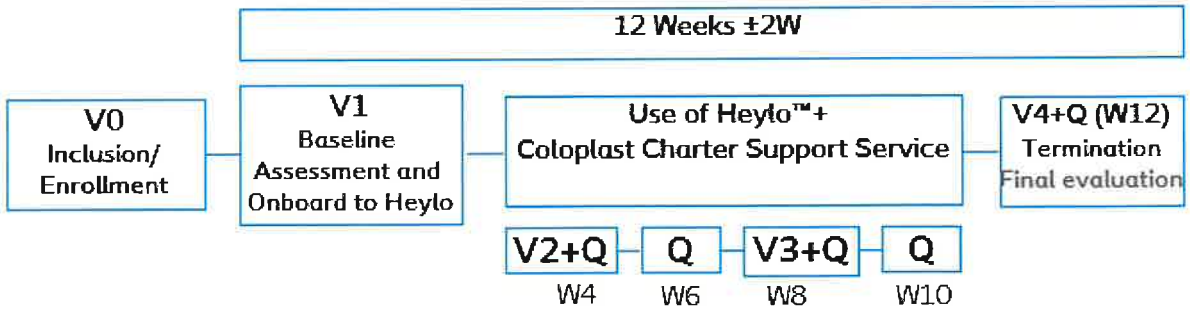
No comparator is used is this study.

5. Design of the clinical investigation

5.1. General

The investigation is a multi-centered, open labelled, single arm case study with an expected duration of the study of 12 weeks ±2 weeks.

The investigation aims to include minimum 60 and maximum 90 subjects within a 6-month recruitment period. Minimum 30 subjects are planned to be enrolled within the 3 months after surgery.



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

Subjects are asked to fill in surveys at baseline and after 4, 6, 8, 10 and 12 weeks of test product use. At V2, V3 and V4 a call from the study nurse will be made to the subjects. In this call study nurse will conduct relevant evaluations together with subject e.g. number of GP contacts, nurse contacts and evaluation of skin (see flow chart section 7.2).

V0: Inclusion

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

V2-V4: Test visits. V4 is also termination visit

Vx: Follow up visits if needed

5.2. Primary endpoint

Primary endpoint *(Overview of question Appendix 8, A)*

- Number of times with stoma effluent leakage outside the baseplate (e.g. onto clothes or bed sheets) within the last 2 weeks.

5.3. Secondary and exploratory endpoints

Secondary endpoints *(Appendix 8, B)*

- Patient Self-management (Patient Activation Measure (PAM), Appendix 3)
  - PAM score (0-100)
- Leakage related QoL (OLI, Appendix 2)
  - Emotional impact score (0-100)
  - Usual/social activities score (0-100)
  - Coping/Control score (0-100)
- Health Related Quality of Life (EQ5D-5L, Appendix 4)
  - EQ-5D-5L – index score (UK)
  - EQ-5D-5L – VAS score

Exploratory endpoints *(Overview of endpoints and questions Appendix 8, C)*

- Skin condition measured by Decision Tree Score (0-3) based on Peristomal Skin Health (OST 2.0) (without pictures) (Appendix 6)
- Quality of Life measured by WHO5 score (0-100) based on Mental wellbeing (WHO5) (Appendix 5)
- Worry about leakage (5-point scale, Appendix 8, C.3)
- Feeling of security (5-point scale, Appendix 8, C.4)

Evaluation of Heylo device (Questions, scale and assessment time Appendix 8, D)

- Technical assurance/ interoperability
  - Reliability and timing of notifications
  - System stability
- Usability/interoperability
  - Usability and ease of use evaluated through System Usability Score (0-100) (Appendix 7)
- Other evaluations of self-management, and self-confidence
  - Easiness in knowing when to change appliance
  - Confidence at night
  - Peace of mind
  - Adverse events

Evaluation of Heylo + Service (Questions, scale and assessment time Appendix 8, E)

- Preference
- Reason for preference
- Future use
- Recommendation to others

Evaluation of Coloplast Charter Support Service (Questions, scale and assessment time Appendix 8, F)

- Calls by subject and by Coloplast Care
- Evaluation of the call
- Frequency of calls
- Recommendation of call service

Evaluation of Heylo by study Nurse (Questions, scale and assessment time Appendix 8, G)

- Easiness of how to onboard to Heylo
- Easiness in how to train subjects in using Heylo
- Evaluation of patient self-management with Heylo
- Evaluation of routines with Heylo
- Recommendation of Test Product

Recurrent Assessments (*Questions, scale and assessment time* Appendix 9)
By subject

- Output consistency (Bristol scale; Appendix 1)
- Baseplate wear time (change pattern)
- Main reason for change
- Use of Accessories
- Unplanned changes due to worry of leakage
- Impact of leakage to work (sick days)

By study nurse

- Readmission (Y/N) + reason (planned/unplanned)
- GP visits (n) + reason during last month
- Nurse visits (n) outside routine/outside study
- Needed baseplate change (Y/N), if Y provide new type/size (ongoing)
- Needed Heylo size change (Y/N), if Y provide new size (ongoing)
- Register contact with Technical Support
- Register if new part is sent to subject

By Call Advisor (ongoing)

- Who calls who (Subject; Call Advisor)
- Main reason for call
- Points discussed with subject
- Recommendations given (tick those that apply)
- Contact to study nurse

By technical support (ongoing)

- Who calls who (Subject; technical assistant)
- Aspects of provided technical support
- Register in Trackwise/Vigilance (N,Y-if device deficiency)
- New part needed (Y/N)
- Contact to study nurse (Y/N)

5.4. Rationale for selection and measurement of endpoints

The endpoint "Number of times with stoma effluent leakage outside the baseplate" has been selected as primary endpoint in this investigation as this is the core performance measure of the Test Product.

Secondary endpoints are related to quality of life and patient self-management, which are important patient health measures, which Test Product may help to improve. All secondary endpoints are measured by validated questionnaires. Ostomy Leakage Impact (OLI) related QoL consists of three domains; Emotional impact score, Usual/social activities and Coping and control, all with scores from 0-100. Patient self-management is measured by Patient Activation Measure (PAM) with a score from 0-100. Health related quality of life is measured by EQ5D-5L with an index score and a VAS score.

Exploratory endpoints are related to subject self-assessment of the peristomal skin condition as well as usability and user's overall wellbeing and experience with Heylo™ system and Coloplast Charter Support Service

5.5. Demography and potential compromising factors

Baseline/demographics (Overview of questions in Appendix 10)

- Gender (male/female)
- Age (at time of enrolment (years)
- Height (cm)
- Weight (kg)
- Date of stoma creation (DD/MM/YYYY)
- Date of discharge from hospital (DD/MM/YYYY)
- Reason for creation of the stoma (Crohn's disease/ulcerative colitis/ cancer/ Other)
- Stoma Type (ileostomy/colostomy)
- Stoma sub-Type (loop/end)
- Shape of the stoma (round/oval/irregular)

- Size of the stoma (widest diameter and height of stoma from skin)
- Body profile
- Information about current stoma product (1P/2P; Flat, convex, concave; Brand)
- Stoma awareness
- Technical ability
- Work status (working, restricted duties, sick leave, unemployed/retired, student)
- Are you using Coloplast Charter Service offering already? (Yes/No)
- Users Phone type (for Heylo App) iPhone Version 6 or newer (software V.13.3+) and Android Version 7 or newer (i.e. Samsung Galaxy) (Software 8.0+)
- Heylo size selected

5.6. Equipment/methods and timing for assessing the variables

Assessment data will be captured at V1, V3 and V4 or between visits by the study nurse who enter the data in the eCRF. Primary, secondary and explorative endpoint data will be captured at baseline and week 2, 4, 6, 8, 10 and 12, by the subject who will enter the data in a subject questionnaire in the EDC system.. Please see flowchart section 7.2 for further information regarding timing of endpoint data capture.

5.7. Total expected duration of the clinical investigation

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

- First subject enrolled (10/2021).
- Last subject enrolled (03/2022).
- Last subject completed (06/2022).
- Final report (06/2023).

6. Clinical Investigation population

The clinical investigation will be conducted in up to n=90 subjects enrolled in up to 10 clinical investigation sites.

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:	Inclusion:
1. Have provide written informed consent	1. To meet the Helsinki Declaration
2. Be at least 18 years of age and have full capacity	2. To meet the Helsinki Declaration
3. Have had their stoma for less than 9 months	3. To investigate the benefits of Test Product in subjects early after surgery
4. Have intact skin on the peristomal area (assessed by investigator)	4. The skin must be intact (anatomical closure of skin with sutures is okay). No broken or bleeding skin, wound, or ulceration and only minor discoloration of the skin.
5. BeBe able to use one of the five Test Products (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm)	5. The technical design of the device requires use of one of the five Sensor layer sizes.
6. Ileo- or colostomists with liquid and/or mushy output (Bristol scale type 5-7), see Appendix 1	6. The sensor design requires output with some moist in it.
7. Is willing to refrain from use of paste and protective sheets	7. Subjects cannot use paste or protective sheets.
8. Have a smartphone applicable for the Heylo™ app.	8. Heylo™ app. needs to be installed on subjects own phones.
9. Have been self-managing stoma appliance for at least 14 days	9. To meet Primary endpoint
10. Are able to follow study procedures for 3 months (assessed by investigator)	10. To ensure low drop-out rate
	11. To be able to receive the Test Product

11. Are willing to receive their ostomy products through Coloplast Charter for the duration of the study.	

6.1.2. Exclusion criteria

Exclusion criteria	Exclusion:
1. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment 2. Is breastfeeding 3. Is pregnant based on urine pregnancy test 4. Enrolled in another current ostomy device study or have previously participated in this investigation. Co-enrolment must be agreed with sponsor. 5. Has known hypersensitivity towards any of the products used in the investigation 6. Is using/have a pacemaker 7. Has a complicated stoma at baseline (dehiscence/prolapse/hernia) 8. Has limited life expectancy or receive palliative care. 9. Has stage 4 cancer. 10. Having more than one stoma synchronously 11. Having ongoing non-healed abdominal wounds 12. Reoperation / stoma reversal planned during the study period	1. Steroid product on peristomal skin may interfere with the skin condition. Use of steroid product can make the skin more fragile to baseplate change. 2. Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown. 3. Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown. 4. Other research study guidelines/products may interfere with these investigational endpoints. 5. To protect subject's wellbeing 6. To protect the subjects from unnecessary harm users with a pacemaker are excluded. 7. These patients represent a complex subpopulation who's experience may skew data and exploration of this group with specific additional needs is beyond the scope of the current study. 8. To minimize drop out 9. Excluded for ethical reasons 10. This would represent a complex abdominal environment and skew interpretation of the results and exploration of this group with specific additional needs is beyond the scope of the study. 11. To protect the subjects from unnecessary harm 12. To minimize drop out

6.1.3. Pregnancy and breastfeeding

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

If the subject becomes pregnant during the investigation, it is important, that the subject informs the Investigator/Investigator representative immediately. The PI will then consider whether she should continue in the investigation.

6.2. Recruitment and enrolment

Recruitment of potential subjects will begin once approval have been obtained from the Research Ethics Committee (REC). It is estimated that the recruitment process will be completed within 6 months.

Table 1: Table showing an overview of the recruitment process.

Recruitment method	[redacted]	[redacted]	[redacted]
Potential subjects	[redacted]	[redacted]	[redacted]
First contact	[redacted]	[redacted]	[redacted]
	[redacted]		
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, 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, at subject's own home or remotely. 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.

6.3. Subject withdrawal criteria

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

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

- Noncompliance with the CIP impacting the scientific integrity of the investigation.
- If subject's safety and wellbeing is compromised by further participation.
- Subjects lost to follow-up. At least three documented attempts will be made to verify subjects lost to follow-up.

Withdrawn subjects will not be replaced by new subjects.

A subject who is withdrawn from the investigation, for any reason, will be encouraged to contact the investigator if problems arise that the subject believes are related to the clinical investigation. Subjects who have not experienced any adverse events will not be followed up. For subjects who experience adverse events, see section 18.5.

6.4. Point of enrolment

A subject is considered enrolled in the investigation at the time at which, following recruitment and before any clinical investigation-related procedures are undertaken, the subject signs and dates the informed consent form. The expected duration for each subject is described in section 5.1.

6.5. Subject Identification and Confidentiality

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

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

The principal investigator for each clinical investigation site will maintain as part of the investigational file a list identifying all subjects enrolled in the clinical investigation.

7. Procedures

7.1. Clinical investigation-related procedures

Visit 0 (V0, Inclusion visit)

If a potential subject is interested in participating after the first contact and they met screening and inclusion criteria, a visit (visit 0) is arranged. When arranging the visit, it will be ensured, that the subject has received the Subject Information Form prior to the visit. The subjects will receive both written and verbal information to ensure that the subject understands what was read and explained and can freely agree to participate in the investigation. The subject will, beforehand, also be informed about the possibility of bringing a companion to Visit 0 and to any possible subsequent visits. During the visit the principal Investigator, or delegate, will provide oral information about the investigation based on the Subject Information Form. The subject has the right to wait before deciding on participation.

If/when subjects decide to participate, they will be asked to sign the Informed Consent Signature Form. Hereafter, relevant female subjects will be asked to take a pregnancy test. If a subject so desires, and it is certain that it is understood what the investigation entails, and the relevant form has been signed, the subjects are considered enrolled in the investigation. Enrolled subjects are allocated a subject number. Visit 0 and visit 1 can be combined.

Visits 1 (V1, Baseline visit)
During visit 1, baseline questions will be completed by the Principal Investigator, or delegate. The subject will be thoroughly trained in the use of the Test Product and the Principal Investigator, or delegate will ensure questions relevant for visit 1 are completed.

Visits 2, 3 and 4 (V2, V3 and V4)
During visit 2, 3 and 4, potential (S)AE's will be captured by the Principal Investigator, or delegate. During visit 2, 3 and 4 the Principal Investigator, or delegate will ensure questions relevant for the given visit are completed. Visit 4 (V4) is also termination visit.

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

7.2. Flow-chart

Table 2 chart showing the connection between visits and assessments.

Assessment	Screening visit (V0)	Visit 1 (V1)	Ongoing	Visit 2 (V2 week 4)	Visit 3 (V3 week 8)	Visit 4 (V4) Week 12)	Survey (Weeks 4, 6, 8, 10 and 12)
Informed consent	X						
Inclusion and exclusion criteria	X						
Pregnancy test (urine dipstick)	X						
Subjects are trained in Investigational product use according to IFU.		X					
Assessment of subject's wellbeing and compliance with CIP	X	X		X	X	X	X
Subject to complete questions in electronic survey		X					X
Study nurse Complete eCRFs	X	X		X	X	X	
Deviations	X	X	X	X	X	X	
Adverse Events		X	X	X	X	X	
Device Deficiencies		X	X	X	X	X	
Concomitant Medications	X	X	X	X	X	X	

7.3. Case Report Forms
All assessments and observations throughout the investigation must be carefully recorded in an EDC (Electronic Data Capture) system. Details about data capture can be found in section 11.1

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

7.5. Supplementary materials and equipment (if applicable)
The Sponsor will provide the Principal Investigator, or delegate with supplementary materials for this investigation. Supplementary materials would be:

- Computer with access to CRFs

8. Risk – benefit analysis and ethical considerations

8.1. Risk-benefit analysis of the investigational device
A risk analysis according to ISO 14971 Application of risk management to medical devices has been conducted. Risks have been proven minimized or eliminated through appropriate design control, confirmed by pre-clinical bench, laboratory and clinical testing.

All unacceptable risks related to the device have been mitigated as far as possible and have been deemed acceptable for the clinical study. The Heylo™ device will be CE marked prior to study start.

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

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

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

Possible benefits for the subjects in this investigation, are that subjects are notified if a leakage occur, which maybe will be beneficial for the subjects in regards to the quality of life and maybe minimize the worry about leakage.

8.3. Risk Analysis for the conduct of the clinical investigation
A risk assessment of the clinical investigation will be conducted initially prior to the first subject enrolment and periodically re-assessed based on any new risks identified through the process. This assessment will be completed throughout the duration of the investigation, as defined by the study team. A risk-based monitoring strategy may be implemented including on-site remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

8.4. Delegation of responsibility
Before initiation of the clinical investigation, sponsor must be provided with key personnel signed and dated curriculum vitae (not more than 2 years old) to verify their qualifications. Key site personnel are those, who treat or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all site personnel are trained in the investigation procedures, how to complete the CRFs, procedure for reporting an adverse event or serious adverse event (how, when, to whom), and who to contact in case of emergency related to the investigational device.

9. Monitoring Plan

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

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

Monitoring activities are mandatory as per good clinical practice, however the extend and depth of these activities depend on the criticality of the clinical investigation, speed of enrolment, the experience of the clinical investigation site personnel in carrying out clinical investigations and specific study designs.

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

9.1.1. Site selection visit

Depending on the prospective clinical investigation sites experience with the specific investigational device, an on-site qualification or site selection visit shall be performed during which the feasibility of the clinical investigation requirements will be discussed and common agreement between sponsor and principal investigator shall be reached. This visit may also be replaced by one or more phone calls if the principal investigator is known to the sponsor.

9.1.2. Initiation visit

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

The initiation visit will be held on site or remotely using Microsoft Teams, Skype or Face time. The initiation visit will be held as close to study start as possible.

9.1.3. Monitoring visit(s)

The site dedicated monitor is to ensure adherence to the clinical investigation plan, accurate data recording on the eCRFs and to monitor recruitment rates and adherence to follow-up schedules. The principal investigator shall permit and assist the monitor to carry out verification of completed eCRFs against data in the source documents.

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

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

The sponsor, or delegate, will provide clinical monitoring, including review of eCRF with verification to the source documentation, as defined in the monitoring plan.

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

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

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

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

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

9.2. Source data verification

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

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

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

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

10. Statistical considerations

10.1. Statistical design, method and analytical procedures

Definition of analysis populations

Intention to Treat (ITT) and Safety populations will be defined at a formal data review meeting 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 subjects with valid informed consent who have been exposed to the Test Product, with information on at least one endpoint.

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

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

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

Analysis of endpoints, individual questions, and assessments

All endpoints and individual questions from questionnaires as well as assessments will be listed and summarized by descriptive statistics. If relevant, the summaries can be done by the information about the current stoma product (1P/2P; Flat, convex, concave; Brand).

The summaries for the endpoints and individual questions will be made for each time point (baseline, Q1, Q2 etc), separately. For relevant endpoints, the summaries will also be done by time since surgery and/or time since discharge from hospital.

Summary 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, summary statistics are presented with N and percentage, where percentage is based on the total number of

subjects/observations with non-missing data. If relevant, the summary statistics can also include a 95% confidence interval for the mean or the calculated percentage.

For the primary endpoint, a paired comparison between data from Visit 4 (or last visit after at least 4 weeks of use of Heylo™) and baseline data (V1) will be performed. If data can be normally distributed the comparison will be performed by a paired t-test.

The secondary and exploratory endpoints can be analyzed similar to the primary endpoint but including time since surgery or time since discharge from hospital as a covariate, if relevant.

Other summaries and analyses can be made, if relevant.

As it is an exploratory study no adjustment for multiple testing will be applied if statistical analyses are performed.

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

10.2. Sample size

The study aims to recruit 60-90 subjects with expected drop-out rate up to 25%. It is assumed that 60-90 included subjects will be adequate for investigating the benefits of Heylo™ delivered together with the online support service.

With 60-90 subjects and a drop-out rate of 25% it is assumed that at least 45 subjects will have information about leakage outside the baseplate at baseline and after at least 4 weeks of using the Test Product. As the distribution of the numbers of leakage outside the baseplate is unknown, the sample size calculation is based on a worst-case calculation where the primary endpoint is evaluated as leakage outside the baseplate with in the last 2 weeks (Yes/No) instead of using the exact number of times with leakage. If this proportion is reduced from 27% at baseline as observed in Nafees 2018 [7] to 3% by end of study, we will have a power of 85% to detect the difference as statistically significant, when using a 2-sided paired exact test in the binomial distribution, testing on a 5% level.

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

10.3. Level of significance and power

When a statistical analysis is performed a 2-sided significance level of 5% will be applied. For information regarding the power see section 10.2.

10.4. Pass/fail criteria

No formal success criteria are applied in this investigation.

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

10.5. Interim analysis

There is no planned interim analysis in this investigation.

10.6. Statistical reason for termination of investigation

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

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

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

11. Data management

11.1. Data collection and data management

11.1.1. Data Collection in the clinical investigation

Data management and statistical analyses of all measurements described in this protocol are carried out by the Medical Affairs, Coloplast A/S.

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

The EDC system used is [redacted]. The system is designed to be compliant with the FDA requirements of 21 CFR part 11. It is a validated data management system allowing only qualified and trained personnel to enter the system. The system has full audit trail and electronic signature.

The Principal Investigator, or delegate, will enter data in a part of the system referred to as the eCRF. The subjects will receive a link to the system to enter their registrations in a part of the system referred to as the subject questionnaire.

The sponsor will be responsible for training the investigator or delegate, in completion of the eCRF.

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

The eCRF will be completed by the investigator, or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log. It will be the responsibility of the investigator to ensure that all measurements and observations are correctly noted in the eCRF.

All assessments and observations throughout the investigation for each subject must be carefully recorded in an eCRF during the visit or immediately after. The eCRF makes it possible to enter data right away when they are obtained. This is the preferred way of collecting data. In case this is not possible the data should be entered no later than 7 days after the visit / procedure.

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

Subject and investigator are required to complete different sections in the CRF. Please see the flow chart 7.2 for details. If needed the investigator will assist the subject in completing the questionnaires.

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

The investigator will keep a separate list of the subjects' ID numbers, names and addresses in a locked room/cabinet. Only data referred to in this clinical investigation plan will be recorded in the CRFs.

11.1.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The principal investigator or delegate must be trained in the system prior to getting access. The training must be completed before access to the investigation is granted. Only the principal investigator, or delegate, will be authorised to enter data in the eCRF.

The monitor, using his/her personal login information shall verify all critical data points against the source documents and issue electronic queries for the authorised clinical site personnel to respond, as defined in the monitoring plan.
The principal investigator, using his/her personal login information shall sign each eCRF.
Automated, real time access to the data enable control on study compliance and safety assessments.

A critical quality control will be performed by the sponsor's data management team and queries issued where needed.

At the end of the study a formal data review meeting will be performed before the database will be locked.

A full audit trail ensures, that each user's (site personnel, monitor, sponsor, data manager) access to and actions in the system is tracked.

The Data Management Procedures are further described in the Data Management SOPs.

11.2. Remote monitoring

Remote (source data verification) and/or centralized (data review) monitoring is carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than the site(s) at which the clinical investigation is being conducted (evaluation without visiting the investigation site). Remote monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

In addition to onsite monitoring visits, remote monitoring of the data entered in the e-CRF system could be used to achieve the following:

- Conduct activities such as: standard checks of range, consistency, and completeness of data and checks for unusual distribution of data, such as too little variance)
- Special attention will be given in case of frequent data anomalies or errors, protocol deviations or excessive dropouts.
- Augment on-site monitoring by performing monitoring activities that can only be accomplished using centralized processes (e.g., statistical analyses to identify data trends not easily detected by on-site monitoring)
- Monitor data quality through routine review of submitted data in real-time to identify missing data, inconsistent data, data outliers, and potential protocol deviations that may be indicative of systemic and/or significant errors in data collection and reporting at the site
- Verify source data remotely, provided that both source data and CRFs can be accessed remotely
- Conduct aggregate statistical analyses of study data to identify subject data that are outliers relative to others and to evaluate individual subject data for plausibility and completeness
- Conduct analyses of site characteristics, performance metrics (e.g., high screen failure rates, high frequency of eligibility deviations, and delays in reporting data), and clinical data to identify early on corrective actions needed for characteristics correlated with poor performance or noncompliance

11.3. Data retention

The Investigator file must be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

12. Amendments to the Clinical Investigation Plan

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

All significant changes require notification to the EC. Substantial changes may require approval from the EC prior to implementation. (Example of significant change: Changes of inclusion criteria, end points or assessment methods)

13. Deviations from the Clinical Investigation Plan

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

A minor deviation is defined as those that do not increase risk or decrease benefit or do not have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data. If a deviation increases risk or decreases benefit and/or; has a significant effect on the subject's rights, safety or welfare and/or has a significant effect on the integrity of the data it is defined as a major deviation and the Investigator must inform the monitor immediately, and the Monitor will report and inform the Clinical Manager or designee immediately.

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

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

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

If any deviations to the investigation plan are detected during the monitoring visit, the Monitor shall ensure the site reports all deviations in the eCRF or on the Deviation log in the Investigator File. Additionally, the monitor must report any deviation noted during the visit in the Periodic Monitoring Report.

Monitor will align with data management in each investigation, how data management will be informed about all deviations.

The following information about the deviation will be collected:

- Date the deviation took place.
- State what the deviation is related to.
- Does the deviation affect data integrity?
- Does the deviation affect the subjects safety?
- Clear and concise description of the event.
- Corrective action taken.

14. Device Accountability

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

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

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

- Date of receipt.
- Identification of each investigational device (batch no./serial no./unique code).
- The expire date, if applicable.

- The date(s) of use.
- Subject identification.
- The date on which the investigational device was returned/explanted from the subject, if applicable.
- The date of return unused, expired or malfunctioning investigational devices, if applicable.

15. Statement of compliance

The clinical investigation is conducted in accordance with:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Brazil, October 2013.
- MDD 93/42/EEC as amended by Directive 2007/47/EC (commonly known as the Medical Device Directive).
- MDR (EU) 2017/745
- ISO 14155:2020 "Clinical Investigation of medical devices for human subjects – Good clinical practices".
- Any applicable regional or national regulations will be specified in the country specific CIP.

15.1. Ethics committee and regulatory authorities

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

Sponsor will notify the relevant regulatory authority and EC(s) concerned of the end of the clinical investigation.

15.2. Data protection

As part of the investigation Coloplast A/S, Holtedam 1, 3050 Humlebaek, Denmark ("Coloplast") will collect and process the personal information the subject provides for the investigation ("subject personal data"). This includes identification and contact information (which may be anonymised depending on the nature of the investigation) as well as information about product usage experience and your health. Coloplast will comply with the EU General Data Protection Regulation (GDPR) and the Danish act on data protection ("databeskyttelsesloven"), including in connection with transfer of data to third countries, cf. chapter V of GDPR, Coloplast will only process the subjects' personal data:

1. To conduct the investigation and carry out related research based on subject consent (primary use), cf. articles 6(1)(a) and 9(2)(a) of GDPR,
2. To comply with applicable legal obligations to e.g. ensure reliability and safety, cf. article 6(1)(c) in conjunction with article 9(1)(i) of GDPR, and
3. If separate consent is given for secondary use of subject personal data, cf. articles 6(1)(a) and 9(2)(a) of GDPR – carry out research outside the clinical protocol to improve Coloplast's products and services, and for use in education.

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

Subject personal data will be kept as long as required under applicable laws and regulations. The EU Medical Device Regulation obligates Coloplast to keep the data for a period of at least ten years after the investigation

is completed, or, in the event that the device is subsequently placed on the market, at least ten years after the last device has been placed on the market. Subject personal data will be deleted at the end of the mandatory retention period.

If the subject has questions or queries regarding Coloplast's handling of personal information, the subject can always contact Coloplast's Data Protection Officer at [redacted]. Complaints related to Coloplast's handling of subject personal information may similarly be sent to the Data Protection Officer, and the subject is also entitled to file a complaint with the relevant supervisory authority, which in the case of Denmark is the Danish Data Protection Agency (www.datatilsynet.dk).

The subject can write to [redacted] at any time to request:

- Access to personal data
- Correction of errors in personal data or to erase personal data
- Limit what can be done with personal data
- To receive personal data in machine-readable format (data portability).
- Withdrawal of consents the subject has given Coloplast to process personal data

15.3. Indemnity

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

15.4. Financial conditions

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

The expenses include the salary to the Principal Investigator and study nurses, the cost of Test Products, shipments, transportation, and gift certificates. The Principal Investigator and study nurses have no financial interest in the investigation. The total budget for the investigation is [redacted], covering 90 participants. The expenses are paid on an ongoing basis. All financial agreements with the investigation sites involved in the clinical investigation will be specified in a sponsor investigator agreement.

Subjects will be paid for their participation in the study and receives a gift voucher equivalent in value to [redacted] per visit 1 to visit 4, and [redacted] per completed survey, in total [redacted] if the subject completes the investigation.

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

16. Informed consent process

Written informed consent is obtained from all subjects participating in the investigation after thorough written and verbal information. The information is given by the investigator or his/her representative in the subjects' native non-technical language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks, or inconveniences and/or expected benefits, all anticipated adverse device effects and then have a minimum of 24h before deciding on participation. The subjects will be informed that their participation is voluntary and that they may leave the investigation at any time, without this having any influence on their further treatment.

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

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

This procedure also applies to informed consent obtained from a subject's legal representative. The procedure cannot waive the subjects' legal rights.

17. Subject compensation

17.1. Compensation in case of injury

Product liability and No-Fault Clinical Investigation Insurance covering the duration of the clinical investigation are in place, to enable compensation in the event of an injury to a participating subject. see section 15.3

Subjects will be compensated for their participating in the clinical investigation as described under Financial conditions 15.4.

18. Adverse events, adverse device effects and device deficiencies

18.1. Adverse events

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

18.2. 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 unlikely related, possible related, probable related or with causal relationship on the adverse event form.

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

Table 2 lists anticipated adverse device effects that may occur.

Table 3 Anticipated adverse device effects and their likely incidence rates.

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

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

18.3. Device deficiency

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

Example: Transmitter not able to charge.

18.4. Serious adverse events (SAE)

A serious adverse event is an adverse event that:

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

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

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

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

These are handled under the serious adverse event reporting.

Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

18.4.1. Serious adverse device effect (SADE)

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

18.4.2. Anticipated serious adverse device effect (ASADE)

Anticipated serious adverse device effect is any event that by its nature, incidence, severity, or outcome has been previously identified in the risk analysis report. In this investigation no SADE are anticipated.

18.4.3. Unanticipated serious adverse device effect (USADE)

An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

18.5. Medical care of subjects

Principal investigator shall ensure that adequate medical care is provided, during and after participation in the clinical investigation, to a subject experiencing an adverse event. All ongoing ADEs, SAEs, SADEs and DDs that could have led to a SAE at subject termination will be followed according to the Risk Benefit analysis (see 8.2) and will be followed until a resolution is addressed for a period of 2 months after subject termination. An ongoing adverse event at subject termination visit is documented as the current status for the adverse event and will not be followed up.

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

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

18.6. Reporting and timelines

18.7. Investigator's reporting responsibilities

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

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

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

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

and the intensity of the event should be considered, as such:

- **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. The Senior Clinical Manager is responsible of informing the Chief Investigation about all SAE's.

Please report to:

Coloplast A/S
Holtedam 1-3
3050 Humlebæk
Denmark

[redacted]

18.8. Sponsors reporting responsibilities

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

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

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

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

18.9. Data Safety and Monitoring Board (DSMB)

The review of all safety data will be conducted on an ongoing basis to identify any potential safety issues. If needed, the coordinating investigator 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 coordinating investigator 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 investigational site. The sponsor or investigator will inform the regulatory authority as appropriate and notify the EC about the termination of the site.

If suspension or termination of the clinical investigation occurs, the investigator(s) will promptly inform the enrolled subjects. Sponsor will provide resources to fulfil the obligations from the CIP for follow-up on the subjects as necessary.

20. Clinical investigation report

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

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

The clinical investigation report must be submitted to EC.

21. Publication policy

Publication policy is specified in Sponsor Investigator Agreement.

21.1. General

The investigation will be registered on a public accessible database, e.g. www.ClinicalTrial.gov, before recruitment of the first subject. The results of the investigation, positive as well as negative, may be communicated by abstracts, posters or oral presentations provided that opportunity is given for sponsor to discuss the contents and any conclusions drawn, before the abstract, paper or visual presentations are finalised. In all cases the subject's identity will remain confidential.

Sponsor will undertake to comment on the draft documents within 30 working days of receipt, but the final decision on the contents and format of the publication from the conclusions drawn, will remain with the authors.

No preliminary results will be published.

Data from the investigation is considered confidential until it is published according to the conditions of this CIP.

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

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

21.2. Joint publication

A joint paper will not be published before all PIs have approved the content of the clinical investigation report. If a site cannot approve the results/conclusions drawn, an independent EC will be asked to review, and all investigators must follow its conclusion.

Decisions regarding authorship credit will follow the "Uniform Requirements for Manuscripts submitted to Biomedical Journals" (the Vancouver group) according to which an author of a publication must fulfil the following criteria:

- Substantial contribution to conception and design, or acquisition of data, or analysis and interpretation of data.
- Drafting the article or revising it critically for important intellectual content.
- Final approval of the version to be published.

Investigators who do not meet all the above criteria for authorship will be listed in the acknowledgment section under the heading "clinical investigators" and their function or contribution described. All persons must give written permission to be acknowledged.

21.3. Individual publication

Individual sites may only publish their own data from the investigation (case histories not included) in the case that:

- No joint publication is planned, or a joint paper has already been published.
- Approval from sponsor has been obtained.

22. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if

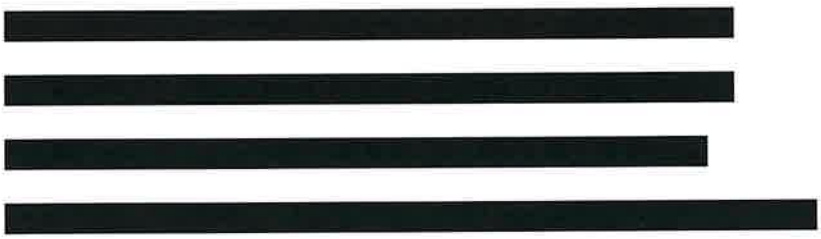
- major non-adherence to the clinical investigation plan is occurring
- it is anticipated that the subject recruitment will not be adequate to meet the investigation objectives [at least 75%] of the subjects should be entered within the recruitment time.

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

23. Bibliography

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

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



[7] [Nafees B et al., The ostomy leak impact tool: development and validation of a new patient-reported tool to measure the burden of leakage in ostomy device users, Health and Quality of Life Outcomes 2018; 16;231

24. Appendix

24.1. Appendix 1 - Bristol scale

The Bristol stool form scale

The stool type illustrations below will help you determine your stool type.

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

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

24.2. Appendix 2 – Leakage scale questionnaire (OLI)

Emotional impact

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

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

Usual and Social activities

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

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

Coping and in control

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

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

24.3. Appendix 3 - Patient Activation Measurement

Below are some statements that people sometimes make when they talk about their health. Please indicate how much you agree or disagree with each statement as it applies to you personally by circling your answer. There are no right or wrong answers, just what is true for you. If the statement does not apply to you, circle N/A.

1.	I am the person who is responsible for taking care of my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
2.	Taking an active role in my own health care is the most important thing that affects my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
3.	I am confident I can help prevent or reduce problems associated with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
4.	I know what each of my prescribed medications do.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
5.	I am confident that I can tell whether I need to go to the doctor or whether I can take care of a health problem myself.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
6.	I am confident that I can tell a doctor or nurse concerns I have even when he or she does not ask.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
7.	I am confident that I can carry out medical treatments I may need to do at home.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
8.	I understand my health problems and what causes them.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
9.	I know what treatments are available for my health problems.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
10.	I have been able to maintain lifestyle changes, like healthy eating or exercising.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
11.	I know how to prevent problems with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
12.	I am confident I can work out solutions when new problems arise with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
13.	I am confident that I can maintain lifestyle changes, like healthy eating and exercising, even during times of stress.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A

24.4. Appendix 4 - Health Related Quality of Life

EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ☒

I have slight problems in walking about ☒

I have moderate problems in walking about ☒

I have severe problems in walking about ☒

I am unable to walk about ☒

SELF-CARE

I have no problems washing or dressing myself ☒

I have slight problems washing or dressing myself ☒

I have moderate problems washing or dressing myself ☒

I have severe problems washing or dressing myself ☒

I am unable to wash or dress myself ☒

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems doing my usual activities ☒

I have slight problems doing my usual activities ☒

I have moderate problems doing my usual activities ☒

I have severe problems doing my usual activities ☒

I am unable to do my usual activities ☒

PAIN / DISCOMFORT

I have no pain or discomfort ☒

I have slight pain or discomfort ☒

I have moderate pain or discomfort ☒

I have severe pain or discomfort ☒

I have extreme pain or discomfort ☒

ANXIETY / DEPRESSION

I am not anxious or depressed ☒

I am slightly anxious or depressed ☒

I am moderately anxious or depressed ☒

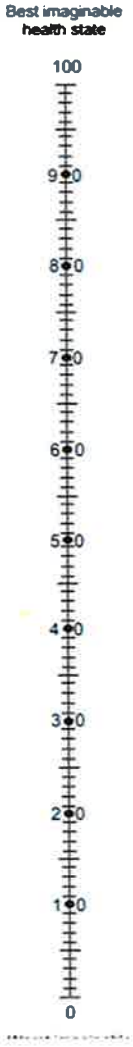
I am severely anxious or depressed ☒

I am extremely anxious or depressed ☒

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health **state is** today.

Your own health state today



24.5. Appendix 5 – Mental wellbeing

WHO-5 Well-being Index

Please respond to each item by marking one box per row, regarding how you felt in the last two weeks.		All of the time	Most of the time	More than half the time	Less than half the time	Some of the time	At no time
WHO 1	I have felt cheerful in good spirits.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
WHO 2	I have felt calm and relaxed.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
WHO 3	I have felt active and vigorous.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
WHO 4	I woke up feeling fresh and rested.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
WHO 5	My daily life has been filled with things that interest me.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

24.6. Appendix 6 – Ostomy Skin Tool (OST) V2.0

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

Patient questionnaire

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

Instructions

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

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

☐	☐
Experiencing	Not experiencing

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

☐	☐
Experiencing	Not experiencing

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

☐	☐
Experiencing	Not experiencing

Instructions

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

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

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

Patient questionnaire

Patient number: _ _ _ _ _ _ _ **Date:** _ _/_ _/_ _ _ _

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

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

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

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

Question 7 (surrogate for picture of skin)

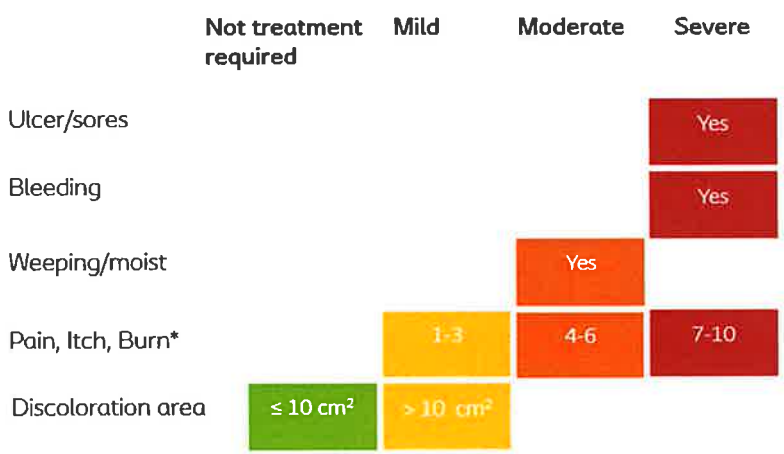
Please evaluate the amount of skin redness in the area around the stoma where your baseplate appliance is placed.

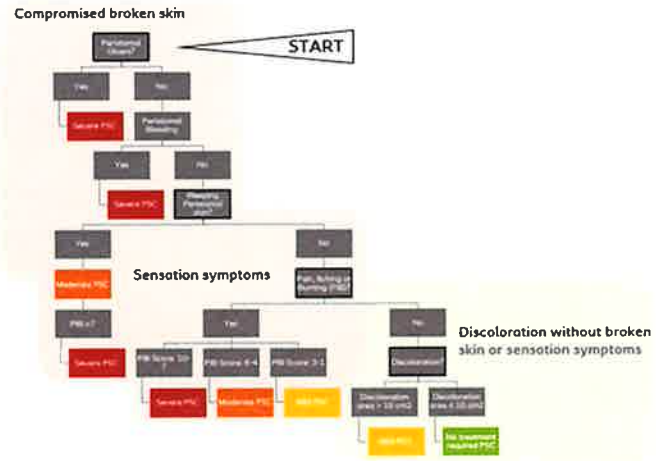
There is no skin redness.

There is skin redness between 0-10 cm^2 (up to around 3cm*3cm)

There is more than 10 cm^2 of skin with redness (one or more areas with redness and total red area larger than 3.5cm*3.5cm)

Ostomy Skin Tool V2.0 - Decision Tree score; subjects will be classified into No treatment required (0), mild (1), moderate (2) or severe (3) skin complications severity level based on the PRO data from OST V2.0 and the skin redness (Question 7)





24.7. Appendix 7 – System Usability Score

System Usability Scale

Instructions: For each of the following statements, mark one box that best describes your reactions to the product *today*.

		Strongly disagree				Strongly agree
1	I think that I would like to use this system frequently.	☐	☐	☐	☐	☐
2	I found the system unnecessarily complex.	☐	☐	☐	☐	☐
3	I thought the system was easy to use.	☐	☐	☐	☐	☐
4	I think that I would need the support of a technical person to be able to use this system.	☐	☐	☐	☐	☐
5	I found the various functions in this system were well integrated.	☐	☐	☐	☐	☐
6	I thought there was too much inconsistency in this system.	☐	☐	☐	☐	☐
7	I would imagine that most people would learn to use this system very quickly.	☐	☐	☐	☐	☐
8	I found the system very cumbersome to use.	☐	☐	☐	☐	☐
9	I felt very confident using the system.	☐	☐	☐	☐	☐
10	I needed to learn a lot of things before I could get going with this system.	☐	☐	☐	☐	☐

24.8. Appendix 8 – Chart of endpoints

No.	Registration/measurements	PERFORMED BY	Visit 1 (0 days)	Visit 2 4 weeks	6 weeks	Visit 3 8 weeks	10 weeks	Visit 4 Termination	Ongoing
	A. Primary endpoint								
A	**Leakages onto clothes** Think back on the last 2 weeks; how many times have you experienced stoma effluent leakage outside the baseplate (e.g. onto clothes or bedsheets)? (number)	Subject	X	X	X	X	X	X	
	B. Secondary endpoint(s)								
B.1	PAM score (0-100) based on Patient Self-management (Patient Activation Measure (PAM)), Appendix 3	Subject	X	X		X		X	
B.2	Emotional impact score (0-100) based on Leakage related QoL (OLI), Appendix 2	Subject	X	X		X		X	
B.3	Usual/social activities score (0-100) based on Leakage related QoL (OLI), Appendix 2	Subject	X	X		X		X	
B.4	Coping/Control score (0-100) based on Leakage related QoL (OLI), Appendix 2	Subject	X	X		X		X	
B.5	EQ-5D-5L – index score (UK) based on Health R QoL (EQ5D-5L), Appendix 4	Subject	X	X		X		X	
B.6	EQ-5D-5L – VAS score based on Health R QoL (EQ5D-5L), Appendix 4	Subject	X	X		X		X	

	C. Exploratory endpoint(s)								
C.1	Skin condition measured by Decision Tree Score (0-3) which is based on subject PRO of Peristomal Skin Health (OST 2.0) (Appendix 6) and inspection of skin redness (no skin redness; <10cm^2; >10cm^2) performed together with Study nurse (Question 7, Appendix 6).	Subject	X	X		X		X	
C.2	WHO5 score (0-100) based on Mental wellbeing (WHO5), Appendix 5	Subject	X	X		X		X	
C.3	**Worry about leakage** Think back on the last 2 weeks, to which degree did you worry about leakage? Very high degree - High degree - Some degree - Low degree - Very low degree/ Not at all	Subject	X		X		X		
C.3.1	**Worry about leakage** **Only answered by subjects who have answered** "Very high degree - High degree - Some degree" worry of leakage (C4). Why did you worry about leakage? (please tick all that apply (odour, embarrassment, soiling of clothes/bed sheets, skin issues, pain, other)	Subject	X		X		X		
C.4	**Feeling of security** How is your feeling of security? Very poor, Poor, Acceptable, Good, Very good		X		X		X		
C5	Adverse Events (see termination form - ongoing)	Nurse							X

D	D. Evaluation of Heylo device								
	Technical assurance/interoperability								
D.1	Reliability of notifications To which degree did you find the notifications from the App reliable and trustworthy? Not at all/Very low degree; Low degree; Some; High degree; Very high degree							X	
D.2	To which degree did you receive notifications timely to react on leakage? Not at all/Very low degree; Low degree; Some degree; High degree; Very high degree							X	
D.3	How stable did you find the overall system in everyday use? Very unstable; Unstable; Somewhat stable; Stable; Very stable	Subject						X	
No.	**Registration/measurements**	**PERFORMED BY**	**Visit 1 (0 days)**	**Visit 2 4 weeks**	**6 weeks**	**Visit 3 8 weeks**	**10 weeks**	**Visit 4 Termination**	**Ongoing**
	Usability/Interoperability								
D.4	System Usability Score (SUS), Appendix 7	Subject						X	
	Evaluation of self-management								
D.5	To which degree did the Test Product make it easier to know when to change baseplate compared to only using usual stoma baseplate? Much lower degree; lower degree; same degree; Higher degree, Much higher degree	Subject						X	
D.6	How was your confidence at night with Test Product compared to only using usual stoma baseplate? Much lower, lower, same, higher, much higher	Subject						X	
D.7	To which degree did the Test Product give you peace of mind? Very low degree; Low degree; Some degree; High degree; Very high degree	Subject						X	

E. Evaluation of Heylo + Service									
E.1	**Preference** Which product solution do you prefer? Stoma appliance alone without Test Product; Stoma appliance with Test Product (Heylo+Service)	Subject						X	
E.2	**Reason for preference** What is your reason for preference? (Please tick all that apply) Body fit; Ability to bend and stretch; Feeling of security; Feeling of confidence; Less fear of leakage onto clothes; Discreet to wear; Discreetness in leakage control; Better sleep; Less embarrassment; Other + text	Subject						X	
E.3	**Future use of product** If the Test Product was available today, would you start using it? (Yes/No)	Subject						X	
E.4	**Recommendation of product to others** How likely would you be to recommend Heylo to other people with ostomy? Not at all/very unlikely: Unlikely; Neither/nor; Likely; Very likely	Subject						X	
F. Evaluation of Coloplast Charter Support Service									
F.1	Did you call Coloplast Charter Support Service during the study period? (Yes; No)	Subject						X	
No.	**Registration/measurements**	**PERFORMED BY**	**Visit 1 (0 days)**	**Visit 2 4 weeks**	**6 weeks**	**Visit 3 8 weeks**	**10 weeks**	**Visit 4 Termination**	**Ongoing**
F.2	Have you received any calls from Coloplast Charter Support Service during the study period? (Yes; No)	Subject						X	
F.3	(if Y in F1 or F2) Did you find the call(s) helpful? Very much, Much; Some; Little; Very little/not at all	Subject						X	

F.4	(if Y in F2) Did you retrieve calls from Coloplast Charter Support Service with an overall acceptable frequency? Yes; No, too many; No, too few	Subject						X	
F.5	How likely would you be to recommend Coloplast Charter Support Service to other people with ostomy? Very likely; Likely; Neither/nor; Unlikely; Very unlikely/ not at all	Subject						X	
	G. Evaluation of Heylo by nurse								
G.1	How was it to onboard subject to Heylo? Very difficult; Difficult; Acceptable; Easy; Very easy	Study nurse						X	
G.2	How was it to train subject in using Heylo? Very difficult; Difficult; Acceptable; Easy; Very easy	Study nurse						X	
G.3	To which degree does Heylo support subject in how to manage their stoma? Very low degree; Low degree; Some degree, High degree, Very high degree	Study nurse						X	
G.4	To which degree does Test Product (Heylo + Service) give subject better routines? Very low degree; Low degree; Some degree, High degree, Very high degree	Study nurse						x	
G.5	Which product would you recommend to your patients? Standard of Care* -- Standard of Care + Test Product (Heylo + Service) -- Standard of Care + Test Product (Heylo + Service) but depends on the health situation of the patient. *Current stoma appliances in the market without Heylo	Study nurse						x	

H. Registration of AE/SAE/termination									
	Registration of termination								
H.1	AEs/ADEs/SAEs/SADEs	Investigator		X		X		X	
H.2	Termination form	Investigator						X	

24.9. Appendix 9 – Chart of recurrent assessments

Registration/measurement	Performed By	Visit 1 0 days	Visit 2 4 weeks	6 weeks	Visit 3 8 weeks	10 weeks	V4 Termination 12 weeks	Ongoing
Recurrent assessments by Subject								
Date filling in **Output type** (Bristol scale, Appendix 1) (V1 and termination) **Weartime** On average, how often did you normally change your baseplate, considering the last 2 weeks? *More than twice per day – twice per day- Once per day -- Every second day -- Every third day --Every fourth day -- Every fifth day -- Every sixth day -- Once a week or less frequent*	Subject	X	X		X		X	

Date filling in **Main Reason for change** What was the main reason(s) for changing the baseplate, considering the last 2 weeks? (Please tick up to three reasons) *I followed my usual changing pattern - There was leakage under and outside the baseplate (soiling the clothes) - Due to a notification from the App - The entire baseplate was detached - The outer edge of the baseplate was detached - The center of the baseplate was detached - I was afraid the baseplate would detach - The area around the stoma was itching - The area around the stoma was painful - There was leakage under the baseplate (but not outside the baseplate - The stoma bag was filled with air - There was a vacuum in the stoma bag - Other*	Subject	X	X		X		X	

Use of accessories (during last 2 weeks) Which stoma accessories did you use, consider the last 2 weeks? (tick all that apply) None; Adhesive remover; Paste; Rings; Ostomy tape; Ostomy belt; Hernia belt; Stoma powder; Barrier lotion/cream/spray/wipes; Cleansing wipes/cleansing spray; Odour remover; Other accessories (please specify) **Unplanned changes due to worry of leakage** Think back on the last 14 days - how many times have you changed the baseplate due to worry of leakage and not due to an actual leakage? Scale with numbers from 0 to 15 **Back to work** Are you back at work (Y/N) If Y. Think back on the last 14 days - how many sick days (number) have you had due to leakage/worry of leakage?	Subject	X	X		X		X	

Registration/measurement	Performed By	Visit 1 0 days	Visit 2 4 weeks	6 weeks	Visit 3 8 weeks	10 weeks	V4 Termination 12 weeks	Ongoing
Recurrent assessments (By study Nurse)								
Was the patient admitted to the hospital since last visit? (registered as AE/SAE on the AE form) What was the number of admissions and number of days admitted?	Study nurse (to summarize at each virtual visit/ call)							
If patient was admitted to hospital since last visit, what was the reason for admission? (collected as AE/SAE on the AE form) **Planned** (scheduled, e.g. re-surgery) VS or **Unplanned** (e.g. dehydration, skin issue, stoma issue)	Study nurse (at each virtual visit/ call)		X		X		X	
Have you seen your general practitioner during last month? Y/N If Y, how many times?	Study nurse (at each virtual visit/ call)	X	X		X		X	

If Y, Was the contact stoma related? (Y/N) If Y to stoma related, please fill in the reason on the AE form Describe reason (example: High Output, fluid loss, weight loss, malnutrition, vitamin deficiency)								
Since last call, have you had <u>any</u> nurse visits <u>outside</u> of routine visits/ outside of those scheduled in study? E.g. visit to hospital nurse or visit from home care nurse? Y/N If Y Frequency	Study nurse (at each virtual visit/ call)	X	X		X		X	
Change of baseplate type/size needed? (Y/N) if Y provide type	Study nurse							X
Change of Heylo size needed? (Y/N), if Y provide new size	Study nurse							X
Have you been in contact with Technical support (Y/N)	Study nurse							X
New part (transmitter/charger) sent to subject (Y/N)	Study nurse							X

Registration/measurement	Performed By	Visit 1 0 days	Visit 2 4 weeks	6 weeks	Visit 3 8 weeks	10 weeks	V4 Termination 12 weeks	Ongoing
Recurrent assessments (By Call Advisor)								
Who called who? Call Advisor Calls Subject --Subject calls Call Advisor	Call Advisor							X
Date of call								X
What was the main reason for the call? Identified problems in Ostomy Check -- Wet mount notification(s) -- First full leakage --Full leakage issues --General leakage issues -- Questions related to Test Product (charger, transmitter, sensor layer) -- Questions related to Test Product app -- Other	Call Advisor							X
Which points were discussed with subject? (tick all that apply) God appliance/ product fit -- Information provided from the Test Product app -- Other aspects related to Test Product -- Accessories use --Leakage issues/how to avoid leakage --Wet mount/ how to avoid wet mount -- Ballooning issues -- Coupling issues -- Skin health -- Adjustment of appliance needs	Call Advisor							X

(accessories) -- Diet and fluid counselling -- Social activities -- Intimacy with a stoma -- Physical activity – Travelling -- Other								
Did the call lead to any recommendations? Yes/No If Yes, which (tick all that apply) Adjustment to change patternChange in accessories use – Change in appliance/product needs Contact to Technical Support (in case of device issue/possible deficiency) -- To contact study Nurse -- To see Stoma Care Nurse -- To see General Practitioner -- Other	Call Advisor							X
Contact to study Nurse Have you contacted the Study Nurse (Y/N)	Call Advisor							X
Registration/measurement	**Performed By**	**Visit 1 0 days**	**Visit 2 4 weeks**	**6 weeks**	**Visit 3 8 weeks**	**10 weeks**	**V4 Termination 12 weeks**	**Ongoing**
Recurrent Assessments (By Technical support)								
Date of call								X

Who called who? Subject called technical support Technical support called subject	Technical support							X
What was the main reason for call with technical support? Transmitter not found -- Parring/re-parring issue -- Connection issue (likely related to sensor layer -- connector/sensor break -- Connection issue (likely related to Bluetooth/wifi loss) -- Error messages -- -- Other If error message, please provide error message number (text field)	Technical support							X
Has the problem been registered in Trackwise/Vigilance? (No, Yes) (if it is a device deficiency/ defect it should be)	Technical support							X
Should a new part (Transmitter/Charger) to be sent to subject? Yes/No	Technical support							X
Contact to study Nurse Have you contacted the Study Nurse (Y/N)	Technical support							X

24.10. Appendix 10 Chart of Baseline assessments

Gender (male/female)

Age (years)

Weight (kg)

Height (cm)

Date of surgery (date, month year)

Date of discharge from hospital (date, month year)

What was the reason for stoma creation? (Crohn's disease/Colitis ulcerosa/ Cancer/ Other)

What is the stoma type? (ileostomy/colostomy)

Stoma sub-type (loop/end)

Shape of the stoma (round/oval/irregular)

Size of the stoma (diameter on widest place and height) (mm)

Which kind of product is normally used?

Flat - Convex – Concave

Which product Brand is normally used? (you may tick more than 1 box) (Coloplast, ConvaTec, Hollister, Dansac, Salts, Welland, Pelican other (text))

What is the product name of the normal ostomy product? (text)

What type of product is normally used? 1-piece -- 2-piece

Stoma awareness

How much of the time are you aware of your stoma?

All of the time (very high awareness) - Most of the time (high awareness) - Some of the time /I sometimes forget (medium awareness) - Rarely /I only think about it once in a while (low awareness) - Never / I don't really think about my stoma (very low awareness)

Technical ability

When it comes to new technology, what describes you best? *I am sceptical and use it only when I have to - I am usually one of the last people I know to use a new technology or tech gadget - I prefer to wait until the prize drops to buy a new technology gadget - I prefer to use or buy when a few other people I know have proven it out - I am not always the first to buy a new gadget but I tend to buy or use it before most other people I know - I love new technology and am among the first to experience with and use them*

Work status

- What is your current work status? Retired -- sick leave -- partial sick leave --unemployed – student – employed/back at work (full time)

Are you using Coloplast Charter Service already? (Yes/No), If No are you using another service? If yes which

Which phone type do you use? (Android/iOS/), version 6, 7, 8, 9,10, XR,11,12, other (text), please specify (space to write free text)

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