# Clinical Investigation Plan

## CP345 The ASSISTER Trial

A r**A**ndomized cro**SS**-over tr**I**al inve**ST**igating H**E**ylo, a novel app driven digital supporting ostomy p**R**oduct

October 2021 – December 2022

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**CHANGE LOG**

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| 1.0 | [redacted] | First approved version |
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## SYNOPSIS OF THE CLINICAL INVESTIGATION

CP345 The ASSISTER Trial – A randomized cross-over trial investigating Heylo, a novel app driven digital supporting ostomy product.

### Test products and comparator:

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

The comparator products in this study are Standard of Care which is defined as subject´s own ostomy product.

### Intended use:

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.

### Objectives:

**Primary objective:** Is to investigate whether Heylo™ can improve the emotional impact (measured by the Leakage scale questionnaire (OLI)), compared to Standard of Care.

**Secondary objective:** Is to evaluate whether Heylo™ can improve participation in everyday and social activities compared to Standard of Care.

### Design of the investigation:

The clinical investigation is an open-labelled, randomized cross over trial evaluating Heylo™ and Standard of Care.

Study visits will be conducted at the subject´s home or through remote virtual calls.

Each of the subjects will have an inclusion visit (V0) and a baseline visit (V1) and two test visits - V2 and V3, including Termination visit carried out by the Principal Investigator, or delegate.

At V1, V2 and V3 the Principal investigator or delegate and the subject will complete questionnaires and every 2nd week the subject will be asked to complete questionnaires. All questionnaires will be completed using a remote electronic data capturing method.

A follow-up call will be scheduled 7 days ±2 days after visit 1 and visit 2 to ensure compliance with the provided Investigational device and study procedures and Insurance of subject's wellbeing. Additional calls/visits may be scheduled if needed, assesses by the PI or delegates, and will be registered as unscheduled visits.

### Expected duration of the clinical investigation:

The expected duration of the investigational period is 16 weeks (±6 days). Each Test period is 8 weeks (±3 days).

### Primary endpoint, Secondary endpoint, and Exploratory endpoints:

**Primary endpoint:** Emotional impact score (scale from 0 - 100) measured by the validated OLI scale evaluated at the end of each test period. *See Appendix 1*

**Secondary endpoint:** Participation in society domain score (scale from 0 - 100) measured by WHODAS evaluated at the end of each test period. *See Appendix 3*

**Exploratory endpoints:**

- Impact on Usual and social activities score (scale from 0-100) measured by the validated OLI scale evaluated at the end of each test period. *See Appendix 1*

- Impact on Coping and in Control score (scale from 0-100) measured by the validated OLI scale evaluated at the end of each test period.
  *See Appendix 1*

- Feeling of security evaluated at the end of each test period. Question: "How was the feeling of security while wearing the product?" Answers: Very poor/Poor/Acceptable/Good/Very good.

- Understanding and communicating domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

- Getting around domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

- Self-care domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period. *See Appendix 3*

- Getting along with people domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period
  *See Appendix 3*

- Life activities (household and work) domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period
  *See Appendix 3*

## Population/subjects

The clinical investigation will be conducted in 144 subjects with ileostomy or colostomy with liquid/mushy output.

To be included in the investigation, the subjects must comply with the criteria presented below.

| **Inclusion criteria:** | **Exclusion criteria:** |
|---|---|
| 1. Has given written consent to participate by signing the Informed Consent Signature Form.<br>2. Is at least 18 years of age and has full legal capacity.<br>3. Has an ileostomy or colostomy with consistent liquid/mushy fecal output (5-7 Bristol scale*)<br>**See appendix 2.*<br>4. Is able to use one of the five test products (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm).<br>5. Has experienced leakage** under the baseplate at least three times within the last fourteen days. **Leakage defined as output seeping under the baseplate" See Appendix 5, Figure 2-5.<br>6. Has worry about leakage to "some degree, high degree, or very high degree" (on a five-point Likert scale: Very low degree/Not at all, Low degree, some degree, High degree, very high degree)<br>7. Is willing to refrain from use of ostomy paste.<br>8. Has a smartphone compatible with the Heylo™ application<br>9. Is able to follow study procedures for 4 months (assessed by investigator or delegate) | 1. Is participating in other clinical investigations or has previously participated in this investigation<br>2. Is pregnant or breastfeeding<br>3. Has known hypersensitivity towards any of the products used in the investigation<br>4. Is using/ has a pacemaker |

## 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 | See section 18.3 |
| 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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# List of personnel involved in the Investigation

## 1.1. Sponsor representatives

| COORDINATING CLINICAL MANAGER | SENIOR BIOSTATISTICIAN |
|---|---|
| [redacted] | [redacted] |
| SENIOR MEDICAL AFFAIRS PROJECT MANAGER | DATA MANAGER |
| [redacted] | [redacted] |
| DIRECTOR OF CLINICAL STRATEGIES | DIRECTOR OF CLINICAL OPERATIONS |
| [redacted] | [redacted] |
| DIRECTOR MEDICAL AFFAIRS, GERMANY | CLINICAL TRIAL MANAGER, GERMANY |
| [redacted] | [redacted] |

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

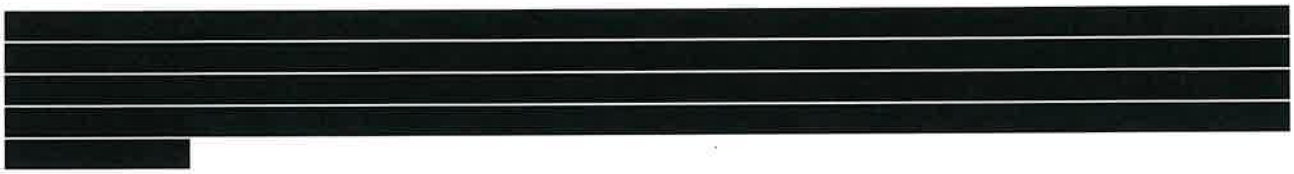
## 1.2. Investigator

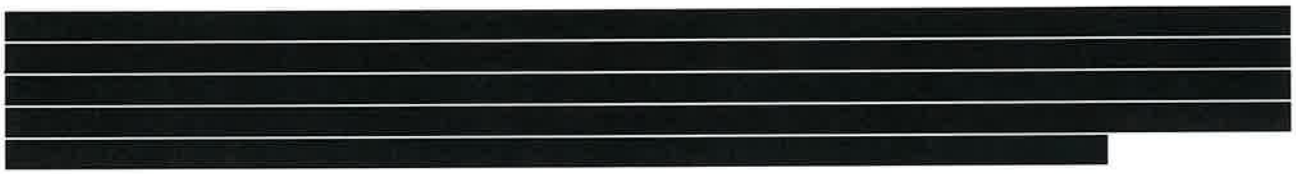
| PRINCIPAL INVESTIGATOR | CONTACT INFORMATION |
|---|---|
| [redacted] | [redacted] |

# 2. Rational/justification for conducting the clinical investigation

People with intestinal stomas (especially an ileostomy) 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 evaluate 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.





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.

The overall aim of this clinical investigation is to evaluate the benefits of the new supporting product, Heylo™ compared to Standard of Care.

# 3. Objectives of the clinical investigation

## 3.1. Objectives

**Primary objective**

Is to investigate whether Heylo™ can improve the emotional impact (measured by the Leakage scale questionnaire (OLI)), compared to Standard of Care.

**Secondary objective**

Is to evaluate whether Heylo™ can improve participation in everyday and social activities compared to Standard of Care.

# 4. Investigational device and comparator

The investigational device is a novel app driven digital supporting ostomy product called Heylo™. Heylo™ is CE-marked.

The investigational device 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.

The comparator in this study will be Standard of Care which is defined as subject´s own ostomy product.

## 4.1. Description of Investigational device – Heylo™

Heylo™ consists of the following:

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

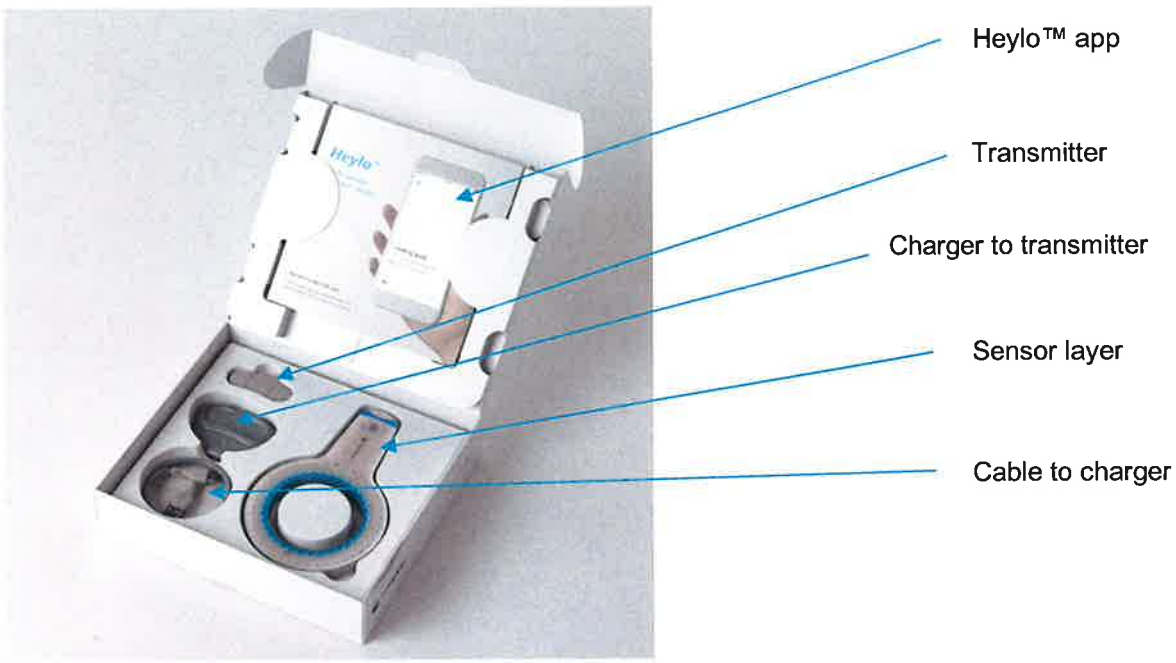



Figure 1: Investigational device - Heylo™

Figure 2: Sensor layer

The colours on the sensor layer (Figure 2) 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 trial: 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

If subjects have technical issues (e.g. technical failure screens delivered to users, and system does not seem to get back running again), they have the possibility to call a technical support service.

### 4.1.1. Manufacturing

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

## 4.2. Identification and traceability of the investigational 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 1.9.2.
  - Android 1.9.2.
- Charger to the transmitter ID 23323072
- Charger cable ID: 23325128

## 4.3. Intended use of the investigational device in the clinical investigation

*Intended purpose of device:*
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 indications:*
The product is indicated for subjects 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 which is attached to the intact peristomal skin around the stoma. The sensor layer detects occurrence of output leakage under the ostomy baseplate and the subject 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].

### 4.4. Intended population for the investigational device
Subjects with an ileostomy or colostomy with liquid/mushy fecal output (5 – 7 on the Bristol scale *See Appendix 2*) and with a certain degree of leakage and worry about leakage, are the intended population for this device.

### 4.5. Handling of the investigational device
The handling of Heylo™ is described in detail in the Instruction for Use (IFU), which is included in all boxes with the investigational device. Storage conditions are also stated in the IFU.

The PI (Principal Investigator) and PI delegate will receive training by sponsor and/or the PI in handling and correct use of the Investigational device. The PI or delegate will train the subjects in the correct use of the investigational device according to the IFU.

### 4.6. Total number of investigational devices intended for the clinical investigation
Each subject will be supplied with Heylo™ app and trial 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

### 4.7. Description of the comparator products
The comparator products in this study are standard of care which is defined as subject´s own ostomy product.

## 5. Design of the clinical investigation

### 5.1. General
The clinical investigation is an open-labelled, randomized cross over trial evaluating Heylo™ and Standard of Care.

Subjects will use Heylo™ together with their own product (Baseplate and bag) during the test period with Heylo™ and in the Standard of Care period subjects will only use their own product (Baseplate and bag).

The expected duration of the total test period is 16 weeks (± 6 days). Each Test period is 8 weeks (±3 days).

In both test periods subjects will change ostomy products as usual, according to their normal change routine. Subjects may decide to change ostomy product earlier or later, based on a leakage notification.


Figure 5: Design of the clinical investigation

In total, 144 subjects will be included and randomized. Each of the subjects will have an inclusion visit (V0) and a baseline visit (V1) and two test visits - V2 and V3, including Termination visit carried out by the Principal Investigator, or delegate.

A follow-up call will be scheduled 7 days ±2 days after visit 1 and visit 2 to ensure compliance with the provided product and study procedures and Insurance of subject's wellbeing. Additional calls/visits may be performed if needed, assesses by the PI or delegates, and will be registered as unscheduled visits.

Before scheduling V0 the subject will be invited to an information meeting , where the PI or Study nurse will give a detailed information about the requirements and the content and what it involves participating in the investigation. The information meeting will be conducted as a phone call. See Section 6.2 for procedure for recruitment and enrolment.

Inclusion visit (V0) and baseline visit (V1) can be performed same day. If subject wishes to reconsider his/her participation at V0 after another oral review of the contents of the trial, the subject has the rights to wait minimum 24 hours before deciding on participation. If subject hereafter decides to participate in the clinical investigation, another date for V0 and V1 will be scheduled.

Study visits will be conducted at the subject´s home or through remote virtual calls.

At V1, V2 and V3 the Principal investigator or delegate and the subject will complete questionnaires and every 2nd week the subject will be asked to complete questionnaires. All questionnaires will be completed using an electronic data capturing method.

V3 will also be the termination visit unless a situation occurs where a subject terminates earlier than expected. If this is the case the subject will as the last visit have the termination visit performed.

## 5.2. Primary endpoint

**Primary endpoint:**

- Emotional impact score (scale from 0 - 100) measured by the validated OLI scale evaluated at the end of each test period.
  *See Appendix 1*

## 5.3. Secondary and Exploratory endpoints

**Secondary endpoint:**

- Participation in society domain score (scale from 0 - 100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

**Exploratory endpoints:**

- Impact on Usual and social activities score (scale from 0-100) measured by the validated OLI scale evaluated at the end of each test period.
  *See Appendix 1*

- Impact on Coping and in Control score (scale from 0-100) measured by the validated OLI scale evaluated at the end of each test period.
  *See Appendix 1*

- Feeling of security evaluated at the end of each test period. Question: "*How was the feeling of security while wearing the product?*" Answers: Very poor/Poor/Acceptable/Good/Very good.

- Understanding and communicating domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

- Getting around domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

- Self-care domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period. *See Appendix 3*

- Getting along with people domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

- Life activities (household and work) domain score (scale from 0-100) measured by WHODAS evaluated at the end of each test period.
  *See Appendix 3*

**Assessments:**

- Leakage outside baseplate, evaluated end of each test period. Question: "*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).*

- Change in current stoma product, evaluated end of test period. Question: "*Has there been any change in current stoma product during the test period?" (Yes/No) If yes, please add: Type (1pc/2pc), Kind (Flat, Convex, Concave), Brand (Coloplast, Hollister, Dansac, Salts, other)*

- Change in Heylo size, evaluated end of test period. Question: "*Change of Heylo size needed?"(Yes/no), if yes, please provide the new size: 40 mm, 50 mm, 60 mm, 70 mm, 80 mm*

- Adverse events/device deficiencies

*For Endpoint and assessment flowchart please see Appendix 4*

## 5.4. Rationale for selection and measurement of endpoints

The primary and secondary endpoints have been chosen as they reflect expected benefits with use of Heylo. The two endpoints consist of the emotional impact domain and participation in everyday and social activities domain, and they are based on validated measurement tools. Evaluation of these quality of life domains as well as other questions related to coping and control, impact on usual and social activities, feeling of security, getting along with people, and life activities may together establish possible benefits of using Heylo compared to using Standard of Care alone.

## 5.5. Baseline information and potential compromising factors

**Baseline/demographics**

- Gender (male/female)
- Age (at time of enrolment (years)
- Height (cm)
- Weight (kg)
- Year of stoma creation (YYYY)
- Ostomy surgery within 3 months (yes/no)
- Reason for creation of the stoma (Crohn's disease/ulcerative colitis/ cancer/ Other)
- Stoma Type (ileostomy/colostomy)
- Temporary/permanent stoma
- Shape of the stoma (round/oval/irregular)
- Size of the stoma (widest diameter and height of stoma from skin)
- Information about the current stoma product: Type (1P/2P), Kind (Flat, convex, concave), Brand (Coloplast, ConvaTec, Hollister, Dansac, Salts, other)
- Working status (working, restricted duties, sick leave, unemployed/retired, student)

## 5.6. Equipment/methods and timing for assessing the variables

Please see Appendix 4 and section 7.1 and 7.2 for information regarding timing of endpoint data capture and section 11. for information on data collection.

## 5.7. Randomization procedure

All subjects that meet the inclusion and exclusion criteria will be randomized into one of two treatment sequences at V1, with a cross-over after 8 weeks (Visit 2). Subjects with stoma surgery less than 3 months, will be stratified according to time since surgery.

Treatment sequences:

Sequence A: Heylo™ + Standard of Care cross-over to Standard of Care

Sequence B: Standard of Care cross-over to Heylo™ + Standard of Care

When testing the Heylo™ it must be done together with subject's usual ostomy product and in the Standard of Care period subjects will only use their own product.

## 5.8. Blinding

No blinding will be used in this investigation, except for the statistician who will be blinded until Data Base Lock.

## 5.9. 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 will be notified.

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

# 6. Clinical Investigation population

This clinical investigation will be conducted in Germany with up to 16 Coloplast Homecare nurses acting as study nurses. In this clinical investigation there will not be an regular Site. The PI who is responsible for conducting the

investigation will delegate study specific procedures to the study nurses, who will perform all study visits at the subjects home.

The clinical investigation will be conducted in 144 subjects with ileostomy or colostomy with liquid/mushy output (5-7 on the Bristol Scale).

The Principal Investigator will be overall responsible for the recruitment for the study and the Clinical manager in Germany will be responsible for the daily contact with the study nurses and the monitoring of the clinical investigation.

## 6.1. Eligibility criteria

To be included in the investigation, the subjects must comply with the criteria presented below.

### 6.1.1. Inclusion criteria

Table 1: Inclusion criteria

| Inclusion criteria<br>To be included in the evaluation a subject must comply with the following inclusion criteria: | | Justification for inclusion criteria |
|---|---|---|
| 1. | **Has given written consent to participate by signing the Informed Consent Signature Form** | To meet the Helsinki declaration |
| 2. | **Is at least 18 years of age and have full legal capacity** | To meet the Helsinki declaration |
| 3. | **Has an ileostomy or colostomy with consistent liquid/mushy fecal output (5-7 Bristol scale*)**<br>***See appendix 2*** | The product is indicated for use with ileostomies and colostomies with liquid fecal output |
| 4. | **Is able to use one of the five test products (i.e. Ø40, Ø50, Ø60, Ø70, Ø80 mm)** | The technical design of the device requires use of one of the five sizes |
| 5. | **Has experienced leakage** under the baseplate at least three times within the last fourteen days.**<br>***Leakage defined as output seeping under the baseplate" See Appendix 5, Figure 2-5*** | To ensure that the subjects have potential leakage which the sensor layer can react upon |
| 6. | **Has worry about leakage to "some degree, high degree, or very high degree" (on a five-point Likert scale: Very low degree/Not at all, Low degree, some degree, High degree, very high degree)** | To ensure only subjects that worry about leakage are included |
| 7. | **Is willing to refrain from use of ostomy paste** | The use of ostomy paste may influence system performance |
| 8. | **Has a smartphone compatible for Heylo™ application** | To answer the CRF questions and handle the Heylo™ applications, the subjects must have smartphones |
| 9. | **Is able to follow study procedures for 4 months (assessed by investigator or delegate)** | To ensure low dropout rate |

### 6.1.2. Exclusion criteria

Table 2: Exclusion criteria

| Exclusion criteria<br>A subject is not allowed to participate in case he/she: | | Justification for exclusion criteria: |
|---|---|---|
| 1. | **Is participating in other clinical investigations or has previously participated in this investigation** | Other investigational guidelines/products may interfere with the investigational endpoints |
| 2. | **Is pregnant or breastfeeding** | Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, foetuses and infants are unknown |
| 3. | **Has known hypersensitivity towards any of the products used in the investigation** | It is not ethical to include persons that know they are allergic to the products used in the investigation and it would also |

| Exclusion criteria<br>A subject is not allowed to participate in case he/she: | | Justification for exclusion criteria: |
|---|---|---|
| | | create bias, as these persons would give the product, they are allergic to a more negative rating and most likely also create an AE. |
| 4. | Is using/ has a pacemaker | To protect the subjects from unnecessary harm, subjects with pacemakers are excluded |

### 6.1.3. Pregnancy and breastfeeding

As specified in exclusion criteria number 2. pregnancy and breastfeeding are not allowed in this clinical investigation. All female subjects with childbearing potential (they have had at least one period during the last 12 months), must at V0 confirm that they are not pregnant or breastfeeding. They will also be informed that no pregnancy is allowed during the investigation.

If the subject becomes pregnant during the Clinical investigation, it is important, that the subject informs the Principal investigator or delegate 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 Ethics Committee (EC). It is estimated that the recruitment process will be completed within 8 months.

Table 3: Table showing an overview of the recruitment process.

| Recruitment method | Coloplast Database |
|---|---|
| Potential subjects | [redacted] |
| First contact | [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 Principal Investigator or delegated will contact the subjects by phone and give a short introduction to the investigation and go over the inclusion and exclusion criteria.<br>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 Principal investigator or a delegated 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 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.<br>See section 16 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 minimum 24 hours before deciding on participation. If/when the subject decides to participate, he/she will be asked to sign the relevant forms (see section 16). |

| | |
|---|---|
| | 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:

- Major 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 when the written informed consent is obtained. 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 (eCRF), and any other document transmitted to the sponsor by the principal investigator or delegate, 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, data monitoring board members or clinical event committee members if involved, members of the EC and if requested to regulatory authorities.

The principal investigator will maintain as part of the investigational file a list identifying all subjects entered into the clinical investigation.

# 7. Procedures

## 7.1. Clinical investigation-related procedures

**Inclusion Visit (V0), Week 0:**

- Introduction to the study and review of Subject information Form
- Informed Consent Form signed
- Inclusion in study and allocation of subject number
- Check of in- and exclusion criteria
- Collect baseline information:
    - Gender (male/female)
    - Age (at time of enrolment (years))
    - Height (cm)
    - Weight (kg)
    - Year of stoma creation (YYYY)
    - Ostomy surgery within 3 months (yes/no)
    - Reason for creation of the stoma (Crohn's disease/ulcerative colitis/Cancer/Other)
    - Stoma Type (ileostomy/colostomy)

- Temporary/permanent stoma
- Shape of the stoma (round/oval/irregular)
- Size of the stoma (widest diameter and height of stoma from skin)
- Information about the current stoma product: Type (1P/2P), Kind (Flat, convex, concave), Brand (Coloplast, ConvaTec, Hollister, Dansac, Salts, other)
- Working status (working, restricted duties, sick leave, unemployed/retired, student)

- Insurance of subjects' wellbeing
- Insurance of subjects' compliance with the CIP

**Baseline Visit (V1), Week 0:**

- Randomization
- Instruct subject in installation of Heylo™ app (on subjects' own smartphone), if relevant
- Instruct subject in completing todays questionnaires:
  - Emotional Impact (OLI)
  - Coping and in control (OLI)
  - Usual and Social activities (OLI)
  - WHODAS 2.0:
    - Understanding and communicating
    - Getting around
    - Self-care
    - Getting along with people
    - Life activities
    - Participation in society
  - Feeling of security, *see section 5.3 and Appendix 4.*

- Assessment of:
  - Leakage outside baseplate, see section *5.3 and Appendix 4.*

- According to the randomization, instruct subject in use of Heylo™ + Standard of Care **or** only Standard of Care for the next 8 weeks
- Provide Investigational device - Heylo™ after measurement of Heylo size, if relevant according to randomization
- Instruct and remind the subject to follow the study specific procedures between visits, and inform subject to complete following questionnaires:
  - Emotional Impact (OLI) every 2nd week
  - Coping and in control (OLI) every 2nd week
  - Usual and Social activities (OLI) every 2nd week
  - Leakage outside baseplate every 2nd week
  - WHODAS- every 4th week
    - Understanding and communicating
    - Getting around
    - Self-care
    - Getting along with people
    - Life activities
    - Participation in society

- Review of AEs, ADEs, SAEs, SADEs, Device deficiencies and protocol deviations
- Schedule follow up call 7 days ±2 days after V1 to ensure compliance with the provided investigational device and study procedures and Insurance of subject's wellbeing.
- Schedule visit 2 in 8 weeks ±3 days

**Visit 2 (V2), Week 8:**

- Insurance of subject's wellbeing and follow-up on subject's compliance with study specific procedures (e.g. completing questionnaires and use of Investigational device + Standard of Care OR Standard of Care only)
- Subject completing todays questionnaires:
  - Emotional Impact (OLI)

- Coping and in control (OLI)
- Usual and Social activities (OLI)
- WHODAS 2.0:
  - Understanding and communicating
  - Getting around
  - Self-care
  - Getting along with people
  - Life activities
  - Participation in society
- Feeling of security, *see section 5.3 and Appendix 4*

- Assessment of:
  - Leakage outside baseplate, see section *5.3 and Appendix 4*
  - Change in current stoma product, see section *5.3 and Appendix 4*
  - Change in Heylo size, if relevant, see section *5.3 and Appendix 4*
  - Review of AEs, ADEs, SAEs, SADEs, Device deficiencies and protocol deviations

- Instruct subject in installation of Heylo™ app (on subjects' own smartphone), if relevant
- According to the randomization, instruct subject in use of Heylo™ + Standard of Care **or** only Standard of Care for the next 8 weeks.
- Provide Investigation device - Heylo™ after measurement of Heylo size, if relevant according to randomization.
- Instruct and remind the subject to follow the study specific procedures between visits, and inform subject to complete following questionnaires:
  - Emotional Impact (OLI) every 2nd week
  - Coping and in control (OLI) every 2nd week
  - Usual and Social activities (OLI) every 2nd week
  - Leakage outside baseplate 2nd week
  - WHODAS- every 4th week:
    - Understanding and communicating
    - Getting around
    - Self-care
    - Getting along with people
    - Life activities
    - Participation in society
- Collect unused Heylo™ devices from subjects who have tested these in the first 8 weeks.
- Collect used Heylo™ devices (only charger and transmitter), from subjects who have tested these in the first 8 weeks
- Schedule follow up call 7 days ±2 days after V2 to ensure compliance with the provided investigational device and study procedures and Insurance of subject's wellbeing.
- Schedule visit 3 in 8 weeks ±3 days

**Visit 3 – Termination Visit (V3), Week 16:**

- Insurance of subject's wellbeing and follow-up on subject's compliance with study specific procedures (e.g., completing questionnaires and use of Investigational device + Standard of Care OR Standard of Care only)
- Subject completing todays questionnaires:
  - Emotional Impact (OLI)
  - Coping and in control (OLI)
  - Usual and Social activities (OLI)
  - WHODAS 2.0:
    - Understanding and communicating
    - Getting around
    - Self-care
    - Getting along with people
    - Life activities
    - Participation in society
  - Feeling of security, *see section 5.3 and Appendix 4*

- Assessment of:
    - Leakage outside baseplate, see section *5.3 and Appendix 4*
    - Change in current stoma product, see section *5.3 and Appendix 4*
    - Change in Heylo size, if relevant, see section *5.3 and Appendix 4*
    - Review of AEs, ADEs, SAEs, SADEs, Device deficiencies and protocol deviations

- Collect unused Heylo™ devices from subject who have tested this in the last 8 weeks
- Collect used Heylo™ devices (only charger and transmitter), from subjects who have tested these in the last 8 weeks
- Termination and completion of the study

**Follow-up call - Performed 7 days ±2 days after visit 1 and visit 2:**

- Ensure compliance with the provided product and study procedures
- Insurance of subject's wellbeing.

## 7.2. Flow-chart

Table 4: Chart showing the connection between visits and assessments.

| | PERFORMED BY | INCLUSION VISIT | BASELINE VISIT | TEST VISIT | TEST VISIT AND TERMINATION VISIT | FOLLOW-UP CALL |
|---|---|---|---|---|---|---|
| **VISIT** | - | **V0** | **V1** | **V2** | **V3/TERMINATION VISIT** | **7 DAYS ±2 AFTER VISIT 1 AND VISIT 2** |
| **WEEK** | - | **WEEK 0** | **WEEK 0** | **WEEK 8** | **WEEK 16** | **WEEK 1 AND WEEK 9** |
| **VISIT WINDOW** | - | - | - | **±3 DAYS** | **±3 DAYS** | - |
| **GENERAL** | | | | | | |
| Review of Subject information | Investigator | X | | | | |
| Signed informed consent Form | Investigator | X | | | | |
| Inclusion and allocation of subject number | Investigator | X | | | | |
| Check of in- and exclusion criteria | Investigator | X | | | | |
| Collect Baseline information | Investigator | X | | | | |
| Insurance of subjects' wellbeing | Investigator | X | X | X | X | X |
| Insurance of subjects' compliance with the CIP | Investigator | X | X | X | X | X |
| Randomization | Investigator | | X | | | |
| Instruction in installation of Heylo™ app and instruction in access to link with questionnaires | Investigator/Subject | | X | X | | |
| **QUESTIONNAIRS** | | | | | | |
| Emotional Impact (OLI) | Subject | | X | X | X | |
| Coping and in control (OLI) | Subject | | X | X | X | |
| Usual and Social activities (OLI) | Subject | | X | X | X | |
| WHODAS 2.0 | Subject | | X | X | X | |
| Feeling of security | Subject | | X | X | X | |
| Leakage outside baseplate | Subject | | X | X | X | |
| Change in current stoma product | Investigator | | | X | X | |
| Change in Heylo size | Investigator | | | X | X | |
| Remind subject to complete questionnaires between visits | Investigator | | X | X | | |
| **PROCEDURES** | | | | | | |
| Instruction in use of Heylo and SoC, according to IFU (if relevant according to randomization) | Investigator | | X | X | | |
| Measure size and provide Heylo (according to Randomization) | Investigator | | X | X | | |
| Collect unused Heylo devices (if relevant) and used charger and transmitter | Investigator | | | X | X | |
| Schedule follow up call 7 days ±2 days after visit 1 and visit 2 | Investigator | | X | X | | |
| Schedule next visit | Investigator | | X | X | | |
| Assess AEs/ADEs/SAEs/SADEs, Device Deficiencies and protocol deviations | Investigator | | X | X | X | X |
| Complete eCRF | Investigator | X | X | X | X | X |

### 7.3. Case Report Forms

All assessments and observations throughout the investigation must be carefully recorded in an electronic CRF (eCRF). Details about data capture can be found in section 11.1

### 7.4. Supplementary materials and equipment (if applicable)

Sponsor will provide the PI, 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 is already CE marked.

### 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 investigational device and the medication participants can take. 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 regard 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 Clinical investigation personnel signed and dated curriculum vitae (not more than 2 years old) to verify their qualifications. Clinical investigation personnel are those, who treat or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all Clinical investigation personnel are trained in the investigation procedures, how to complete the eCRFs, 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 PI and the study nurses.

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 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

An initiation visit with full training on all aspects of the clinical investigation will be provided.
The initiation visit will be held as a physical meeting or remotely using Microsoft Teams, Skype or Face time and the visit will be held as close to study start as possible.

### 9.1.3. Monitoring visits

The sponsor shall determine the extent and nature of monitoring appropriate for the clinical investigation based on the risk assessment. The sponsor shall ensure, through oversight of the clinical investigation and timely adverse event reporting, that unanticipated adverse device effects are identified and investigated rapidly so that, where necessary, additional risk control measures can be implemented.

The dedicated monitor is to ensure adherence to the clinical investigation plan, the safety of the subjects, accurate data recording on the e-CRFs and to monitor recruitment rates and adherence to follow-up schedules. During the clinical investigation, monitors shall check that appropriate written informed consents have been obtained. The principal investigator shall permit and assist the monitor to carry out verification of completed e-CRFs against data in the source documents.

The principal investigator can delegate tasks to his collaborators, however the roles and responsibilities as time period of involvement for each clinical investigation personnel must be documented on the Site Personnel signature and Delegation list as well as training received before getting involved with the clinical investigation must be documented in the Clinical Investigation Training Log.

The monitor shall inform the sponsor about any problems relating to facilities, technical equipment, or medical staff involved in the clinical investigation. The monitor shall also be responsible for notifying such deficiencies in writing to the principal investigator and convene with the clinical investigation 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 below.

The monitor shall make written reports to the sponsor, including documentation of any deviations after each visit and provide written follow up action items if any, to the principal investigator and/or clinical investigation personnel.

All data collected can be directly entered in the eCRF and the Smart Trial system will by 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 Form and AE/ADE will be 100% monitored for timely completeness.

Only the investigator, delegated clinical investigation personnel and the sponsor representatives will have access to all the eCRF´s.

## 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 clinical investigation 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 clinical investigational 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

The primary objective will be evaluated by analysing the primary endpoint whereas the secondary objective will be evaluated by analysing the secondary endpoint. The analyses of the exploratory endpoints will be used to further evaluate and explore the primary and secondary objectives.

All baseline measurements, endpoints and assessments will be summarized by descriptive statistics and/or listed. Endpoints and assessments will be summarized by product and time for evaluation, if relevant. Descriptive statistics for continuous variables are presented with N, Mean, SD (standard deviation), Median, Min and Max, where N denotes the number of subjects contributing with non-missing data. For discrete variables, descriptive statistics are presented with N and percentage, where percentage is based on the total number of subjects/observations with non-missing data.

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

### 10.1.1. Definition of analysis populations

Intention to Treat (ITT) 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 randomised subjects with valid informed consent who have been exposed to at least one 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.

### 10.1.2 Statistical analysis of the primary endpoint

The Emotional impact score (scale from 0-100) measured every 2nd week will be analysed by a linear mixed model. The model includes a fixed effect of product (standard of care, Heylo™), a fixed effect of time (2, 4, 6 and 8 weeks), a fixed interaction between product and time, a fixed period effect and a random effect of subject.

The difference between standard of care and Heylo™ at week 8 will be estimated and tested (the primary comparison). Other combinations of differences can be estimated, if relevant.

### 10.1.3. Statistical analysis of the secondary endpoint

Participation domain score (scale from 0-100) measured by WHODAS will be analysed by a similar model as the primary endpoint except that the questions are only filled out after 4 and 8 weeks.

### 10.1.4. Statistical analysis of the exploratory endpoints

Impact on Usual and social activities score (scale from 0-100) and Impact on Coping ad Control score (scale from 0-100) will be analysed by the same model as for the primary endpoint.

The 3 domain scores based on the WHODAS questionnaires (scale from 0-100) will be analysed by a similar model as the primary endpoint except that the questions are only filled out after 4 and 8 weeks.

Feeling of security evaluated at the end of each test period (5-point Likert scale) will be analysed by a generalized linear mixed model, namely a proportional odds model. The model includes a fixed effect of product (standard of care, Heylo™) and a random subject effect.

### 10.1.5. Adjustment for multiplicity

The results from the analyses of the primary and secondary endpoint will be adjusted for multiple testing by a Bonferroni correction to keep a family-wise type 1 error of 5%. The Bonferroni correction for 2 endpoints correspond to evaluate the difference between products as significant if the p-value is less than 0.025. For the analysis of the exploratory endpoints no adjustment for multiple testing will be applied.

## 10.2. Sample size

The Emotional impact score (scale from 0-100) will be measured every 2nd week and all measurements will be part of the primary analysis whereas the primary comparison will be evaluated at the end of each test period.

The sample size calculation is based on a simplified model (paired 2-sided t-test). The result of the analysis will be adjusted for multiple testing and therefore a test level of 0.025 will be applied in the sample size calculation. Based on data from the previous CP308 investigation (PP population), it is assumed that the total standard deviation of the primary endpoint is 20.6 and that the total variation $20.6^2$ is divided so that the residual variation is $14.4^2$.

Based on the above assumptions 108 subjects should answer the questionnaires at the end of each test period to ensure a power of 81%, if the true difference between the two treatments (with and without Heylo™) is 6 (minimal important difference is in the range of 5-10 according to the validation of the OLI score) [7]. To take a potential drop-out (25%) into account it is recommended to include 144 subjects.

## 10.3. Level of significance and power

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

## 10.4. Pass/fail criteria

The purpose of the investigation is fulfilled if a statistically significant improved mean difference in the primary or secondary endpoint is obtained with the test product compared to Standard of Care.

## 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 the final 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 on electronic Case Report Form (eCRF), 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 will perform primary data collection directly into the eCRF or drawn from source-document (medical records) reviews. The eCRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up.

The eCRF will be completed by the investigator, or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log. It will be the responsibility of the Principal Investigator 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.

In the unforeseen situation, where clinical investigation personnel 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 investigation personnel to respond, as defined in the monitoring plan.
The principal investigator, using his/her personal login information shall sign each eCRF.
Automated, real time access to the data enable control on study compliance and safety assessments.

A critical quality control will be performed by the sponsor's data management team and queries issued where needed. Such queries will be reviewed by the monitor and must be resolved by the clinical investigation personnel.

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

A full audit trail ensures, that each user's ( clinical investigation 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 monitoring is a remote evaluation carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than where the Principal Investigator or clinical investigation personnel is located. Remote monitoring processes can provide many of the capabilities of monitoring as well as additional capabilities.

In addition to monitoring visits at the Principal Investigator or clinical investigation personnel's location, remote monitoring of the data entered in the eCRF 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 monitoring at PI location by performing monitoring activities that can only be accomplished using centralized processes (e.g., statistical analyses to identify data trends not easily detected)
- 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
- 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 don't increase risk or decrease benefit or don't have a significant effect on the subject's rights, safety, or welfare; and/or on the integrity of the data. If a deviation increases risk or decreases benefit and/or; has a significant effect on the subject's rights, safety, or welfare and/or has a significant effect on the integrity of the data it is defined as a major deviation and the Investigator must inform the monitor immediately, and the Monitor will report and inform the Clinical Manager or designee immediately.

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

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

The Clinical investigation personnel 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 subject's 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.

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 Clinical investigation plan and/or other relevant documents are submitted to the appropriate EC. 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.

Sponsor will notify the relevant regulatory authority and EC 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 your personal data to the third parties, but solely for the specified purposes and with the third parties acting on instruction from Coloplast. Data may be collected and processed across the Coloplast network, which may entail processing of personal data outside the European Economic Area. In such cases, an adequate level of protection will be ensured by the third parties being subject to the standard contractual clauses on data protection adopted by

the EU or to an EU-approved certification mechanism on data protection. For further information about this please the subject can always consult Coloplast's data protection officer (details below).

Subject personal data will be kept as long as required under applicable laws and regulations. The EU Medical Device Regulation obligates Coloplast to keep the data for a period of at least ten years after the investigation is completed, or, in the event that the device is subsequently placed on the market, at least ten years after the last device has been placed on the market. Subject personal data will be deleted at the end of the mandatory retention period.

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

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

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

### 15.3. Indemnity

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

### 15.4. Financial conditions

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

The expenses include the salary to the Principal Investigator, the cost of external clinical support, study supplies, eCRF (Smart Trial), Investigator training meeting and travel expenses for nurses attending the Investigator meeting and patient expenses (including travel expenses). The Principal Investigator and study nurses have no financial interest in the investigation. The total budget for the investigation is [redacted], covering 144 participants. The expenses are paid on an ongoing basis.

Subjects will be paid for their participation in the study, and they will receive the payment via bank transfer. to the amount will be [redacted] per visit 1 to visit 3, and [redacted] per follow-up call /after V1 and V2), in total [redacted] if the subject completes the investigation. Payment will be done after visit 3 unless subject terminates earlier.

## 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

## 17.2. Compensation for participating in the clinical investigation

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 comparator(s), or the procedures involved. The adverse event shall be marked with the intensity mild, moderate or severe. This could include events such as headache or dizziness.

## 18.2. 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 5 lists anticipated adverse device effects that may occur.

Table 5: 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 or comparator with respect to its identity, quality, durability, reliability, usability, safety, or performance. This includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labelling.

*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 effect that by its nature, incidence, severity, or outcome has been previously identified in the risk analysis report.

### 18.4.3. Unanticipated serious adverse device effect (USADE)

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

## 18.5. Medical care of subjects

Principal investigator shall ensure that adequate medical care is provided, 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 or delegate 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 must assess all (S)AE`s that occurs during the investigation.
- All serious adverse events and serious adverse device effects must be reported to sponsor within 24 hours of the Clinical investigation personnel 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 clinical investigation personnel 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 clinical investigation personnel 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.

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 the investigator 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 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, sponsor will suspend or terminate the conduct of the investigation. The sponsor or investigator will inform the regulatory authority as appropriate and notify the EC about the termination.

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 Principal 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.

## 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

[redacted]

[5] IFU master approved for CE mark, Doc No: VV-0331823

[6] IFU Master Heylo sensor layer for CE mark, Doc No: VV-0331824

[7] Nafees B, Størling ZM, Hindsberger C, Lloyd A. 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 Qual Life Outcomes 2018 Dec 14;16(1):231.

# 24. Appendix

## 24.1. Appendix 1: 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 |

## 24.2. Appendix 2: 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

## 24.3. Appendix 3: WHODAS 2.0

# WHODAS 2.0

WORLD HEALTH ORGANIZATION
DISABILITY ASSESSMENT SCHEDULE 2.0

## 36-item version, self-administered

This questionnaire asks about difficulties due to health conditions. Health conditions include diseases or illnesses, other health problems that may be short or long lasting, injuries, mental or emotional problems, and problems with alcohol or drugs.

Think back over the past 30 days and answer these questions, thinking about how much difficulty you had doing the following activities. For each question, please circle only one response.

| In the past 30 days, how much difficulty did you have in: | | | | | | |
|---|---|---|---|---|---|---|
| **Understanding and communicating** | | | | | | |
| D1.1 | Concentrating on doing something for ten minutes? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D1.2 | Remembering to do important things? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D1.3 | Analysing and finding solutions to problems in day-to-day life? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D1.4 | Learning a new task, for example, learning how to get to a new place? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D1.5 | Generally understanding what people say? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D1.6 | Starting and maintaining a conversation? | None | Mild | Moderate | Severe | Extreme or cannot do |
| **Getting around** | | | | | | |
| D2.1 | Standing for long periods such as 30 minutes? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D2.2 | Standing up from sitting down? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D2.3 | Moving around inside your home? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D2.4 | Getting out of your home? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D2.5 | Walking a long distance such as a kilometre [or equivalent]? | None | Mild | Moderate | Severe | Extreme or cannot do |

*Please continue to next page ...*

WHODAS 2.0
WORLD HEALTH ORGANIZATION
DISABILITY ASSESSMENT SCHEDULE 2.0



| In the past 30 days, how much difficulty did you have in: | | | | | | |
|---|---|---|---|---|---|---|
| **Self-care** | | | | | | |
| D3.1 | Washing your whole body? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D3.2 | Getting dressed? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D3.3 | Eating? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D3.4 | Staying by yourself for a few days? | None | Mild | Moderate | Severe | Extreme or cannot do |
| **Getting along with people** | | | | | | |
| D4.1 | Dealing with people you do not know? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D4.2 | Maintaining a friendship? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D4.3 | Getting along with people who are close to you? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D4.4 | Making new friends? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D4.5 | Sexual activities? | None | Mild | Moderate | Severe | Extreme or cannot do |
| **Life activities** | | | | | | |
| D5.1 | Taking care of your household responsibilities? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.2 | Doing most important household tasks well? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.3 | Getting all the household work done that you needed to do? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.4 | Getting your household work done as quickly as needed? | None | Mild | Moderate | Severe | Extreme or cannot do |

*Please continue to next page ...*

If you work (paid, non-paid, self-employed) or go to school, complete questions D5.5–D5.8, below. Otherwise, skip to D6.1.

| Because of your health condition, in the past 30 days, how much difficulty did you have in: | | | | | | |
|---|---|---|---|---|---|---|
| D5.5 | Your day-to-day work/school? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.6 | Doing your most important work/school tasks well? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.7 | Getting all the work done that you need to do? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D5.8 | Getting your work done as quickly as needed? | None | Mild | Moderate | Severe | Extreme or cannot do |

| Participation in society | | | | | | |
|---|---|---|---|---|---|---|
| In the past 30 days: | | | | | | |
| D6.1 | How much of a problem did you have in joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.2 | How much of a problem did you have because of barriers or hindrances in the world around you? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.3 | How much of a problem did you have living with dignity because of the attitudes and actions of others? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.4 | How much time did you spend on your health condition, or its consequences? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.5 | How much have you been emotionally affected by your health condition? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.6 | How much has your health been a drain on the financial resources of you or your family? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.7 | How much of a problem did your family have because of your health problems? | None | Mild | Moderate | Severe | Extreme or cannot do |
| D6.8 | How much of a problem did you have in doing things by yourself for relaxation or pleasure? | None | Mild | Moderate | Severe | Extreme or cannot do |

*Please continue to next page ...*



WHODAS 2.0
WORLD HEALTH ORGANIZATION
DISABILITY ASSESSMENT SCHEDULE 2.0

36
Self

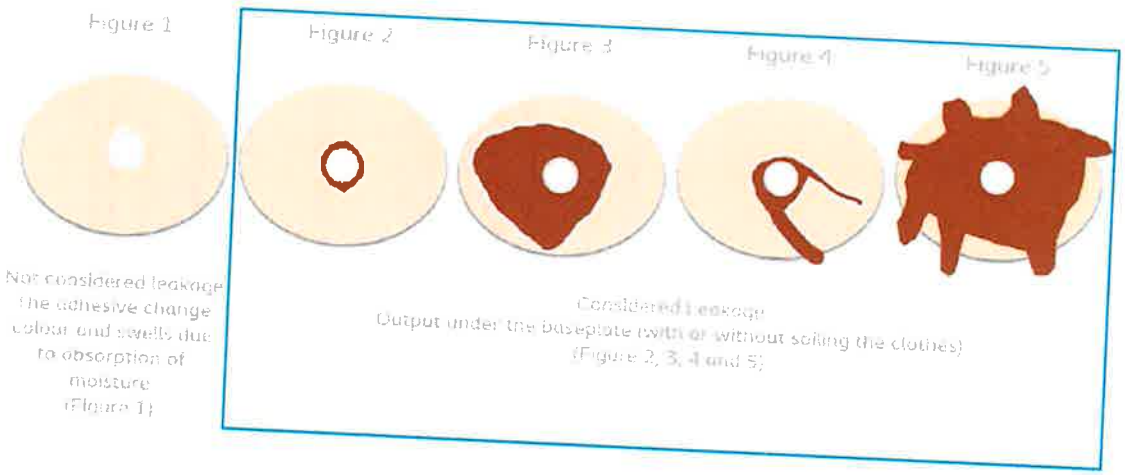
| H1 | Overall, in the past 30 days, how many days were these difficulties present? | *Record number of days ____* |
|---|---|---|
| H2 | In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition? | *Record number of days ____* |
| H3 | In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition? | *Record number of days ____* |

This completes the questionnaire. Thank you.

## 24.4. Appendix 4: Endpoints and assessment flowchart

| | Endpoints and assessment | Assessed by | V1 | V2 | V3 | Every 2nd week | Every 4th week |
|---|---|---|---|---|---|---|---|
| Primary endpoint | Emotional impact score<br>OLI scale – Appendix 1. | Subject | X | X | X | X | |
| Secondary endpoint | Participation in society domain score<br>WHODAS – Appendix 3. | Subject | X | X | X | | X |
| Exploratory end-points | Impact on coping and in control score<br>OLI scale – Appendix 1. | Subject | X | X | X | X | |
| | Impact on usual and social activities score<br>OLI scale – Appendix 1. | Subject | X | X | X | X | |
| | Feeling of security - Question: *"How was the feeling of security while wearing the product?"* Answers: Very poor/Poor/Acceptable/Good/Very good. | Subject | X | X | X | | |
| | Understanding and communicating domain score<br>Getting around domain score<br>Self-care domain score<br>Getting along with people domain score<br>Life activities (household and work) domain score<br>WHODAS – Appendix 3. | Subject | X | X | X | | X |
| Assessments | Leakage outside baseplate – Question: *"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 | |
| | Change in current stoma product – *Question: "Has there been any change in current stoma product during the test period? (Yes/No) If yes, please add: Type (1pc/2pc), Kind (Flat, Convex, Concave), Brand (Coloplast, Hollister, Dansac, Salts, other)"* | Investigator | | X | X | | |
| | Change in Heylo size – Question: *"Change of Heylo size needed? (Yes/no), if yes, please provide the new size: 40 mm, 50 mm, 60 mm, 70 mm, 80 mm"* | Investigator | | X | X | | |
| | Adverse events/device deficiencies | Investigator | X | X | X | | |

## 24.5. Appendix 5: Definition of inclusion criteria: "Leakage defined as output/seeping under the baseplate"



Signature Page for [redacted] v1.0

| | |
|---|---|
| Approved | [redacted]<br>Clinical Manager<br>Medical / Clinical<br>18-Aug-2021 10:23:03 GMT+0000 |
| Approved | [redacted]<br>Director, Clinical Operations Management<br>18-Aug-2021 11:51:37 GMT+0000 |
| Approved | [redacted]<br>Senior Medical Affairs Project Manager<br>Medical / Clinical<br>18-Aug-2021 13:58:08 GMT+0000 |
| Approved | [redacted]<br>Senior Biostatistician<br>Medical / Clinical<br>18-Aug-2021 14:51:01 GMT+0000 |
| Approved | [redacted]<br>Clinical Trial Manager<br>Medical / Clinical<br>18-Aug-2021 16:20:00 GMT+0000 |
| Approved | [redacted]<br>Clinical Manager<br>Medical / Clinical<br>19-Aug-2021 05:35:13 GMT+0000 |

Signature Page for [redacted] v1.0
Document Owner: [redacted]