Coloplast

Clinical Investigation Plan

CP267_01

Evaluation of the Peel Force of New Adhesives From the Skin

June 1, 2021
NCT03200444

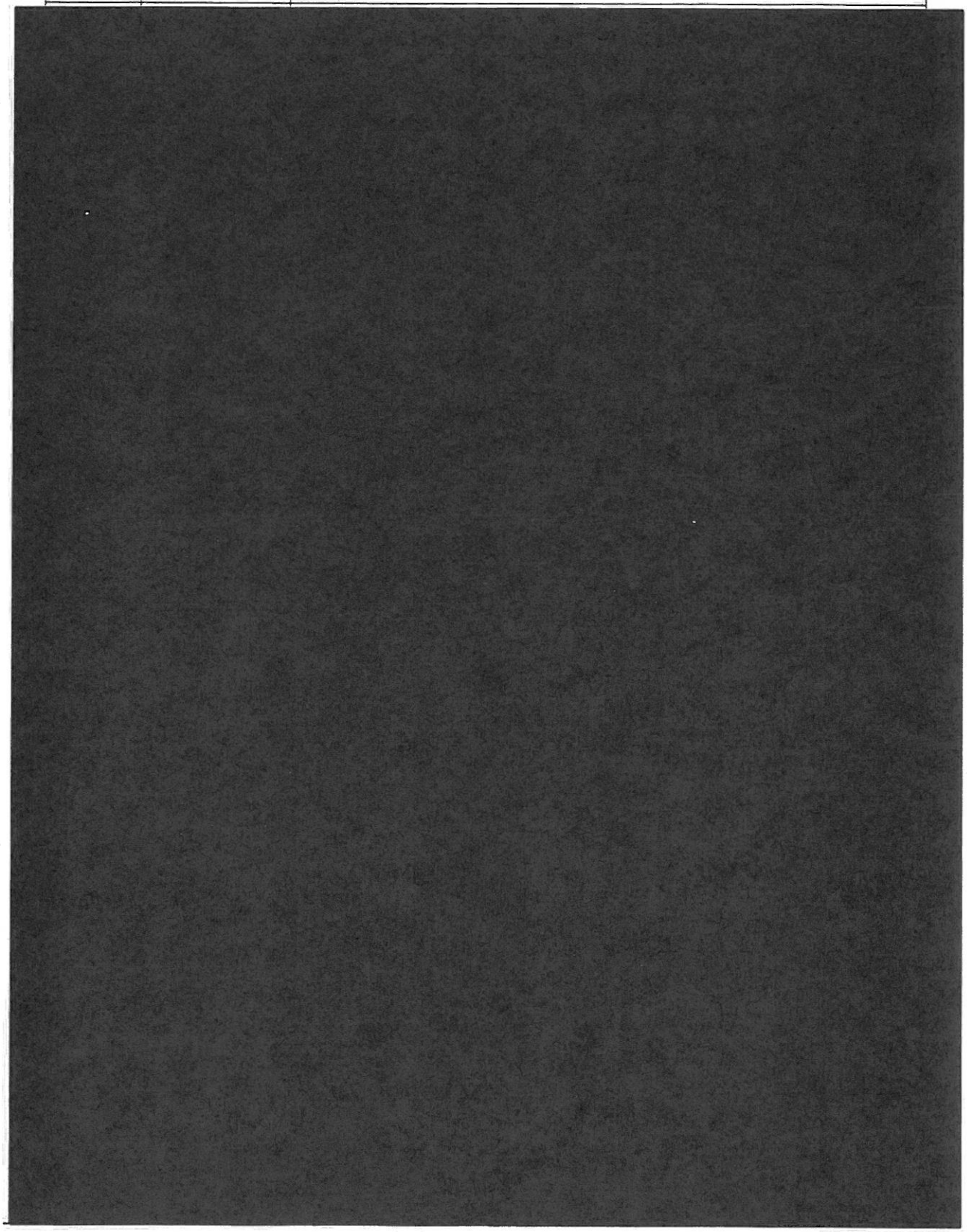
May 2016 – June 2021

Master

Coloplast

CHANGE LOG

VERSION NUMBER	ISSUED BY & DATE	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)



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> SYNOPSIS OF THE CLINICAL INVESTIGATION

Objectives

The primary objective is to investigate water absorption in different adhesives.

Secondary objectives are

- To investigate the impact that different water absorption properties in adhesives have on the initial adhesion, adherent area and skin when applied to skin exposed to buffer, output (simulated in part A and real/simulated output in part B of the study) as well as to dry skin.
- To investigate the impact that different water absorption properties in adhesives have on the adhesion during use with and without conducting exercise (part A and B).
- To explore the variations of adhesive properties when applied to peristomal skin and abdominal skin (part B)
- To explore the variations in water loss and hydration between peristomal skin and abdominal skin (part B)

Primary endpoint and secondary endpoint(s)

Primary endpoint:

1. Swelling of adhesive strips measured by weight (Difference between weight of strip before and after test)

Secondary endpoints:

2. Peel force needed to peel off adhesive strip (assessed when possible)
3. Adherent area on adhesive strip assessed by photos and measured by area (cm^2) or ordinal point scale ranging from very small to very large.
4. Trans Epidermal Water Loss (TEWL)
5. Hydration measured by conductance
6. Redness of skin (erythema) assessed by spectrophotometric method and photos and potential video sequences
7. pH of skin
8. Discomfort when adhesive strip is peeled off and discomfort during use of adhesive strips

Pass/fail criteria

No formal success criteria are applied in this explorative investigation. The investigation will provide valuable insight into water absorption properties of different adhesives and to which degree these impact the adhesion and skin as well as insights to a potential resemblance between abdominal and peristomal skin.

Design of the investigation

The investigation is open-labelled and is divided into two parts: Part A evaluates the adhesive strips on abdominal skin in healthy volunteers while part B evaluates the adhesive strips on peristomal and abdominal skin in people with a stoma.

Population
Part A:

Inclusion criteria:

1. Have given written informed consent

2. Be at least 18 years of age and have full legal capacity

3. Have intact skin on the area used in the investigation

Exclusion criteria

1. Currently receiving or have within the past 2 months received radio- and/or chemotherapy
2. Currently receiving or have within the past months received topical steroid treatment in the abdominal skin area or systemic steroid (tablet/injection) treatment.
3. Are pregnant or breastfeeding
4. Have dermatological problems in the abdominal area (assessed by investigator)

Part B

Inclusion criteria:

1. Have given written informed consent

2. Be at least 18 years of age and have full legal capacity

3. Have had a stoma for more than one year

4. Has an ostomy with a diameter up to 35 mm

5. Have intact skin on the area used in the investigation

Exclusion criteria

1. Currently receiving or have within the past 2 months received radio- and/or chemotherapy

2. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment.

3. Are pregnant or breastfeeding

4. Have dermatological problems in the area used in the investigation (assessed by investigator)

Test products
The study includes a range of different adhesive strips with different water absorption properties.

Investigation approval
Adhesive strips are not considered medical devices and therefore, approval of the clinical investigation from the competent authorities is not deemed necessary.

> LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION	EXPLANATION (IF APPLICABLE)
ADE	Adverse Device Effect	See section 14.3.3
AE	Adverse Event	See section 14.3.3
ASADE	Anticipated Serious Adverse Device Effect	See section 14.3.3
CIP	Clinical Investigation Plan	
CRF	Case Report Form	Questionnaire to be used for data collection
CM	Clinical Manager	
DQF	Data Query Forms	A DQF is specifically used in clinical research. The DQF is the primary data query tool used by the sponsor to clarify discrepancies and ask the investigator for an explanation. The DQF is part of the data validation process in a clinical investigation.
EC	Ethics Committee	
IB	Investigator's Brochure	Compilation of the current clinical and non-clinical information on the investigational medical device(s,) relevant to the clinical investigation.
IFU	Instructions 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 14.3
SAE	Serious Adverse Event	See section 14.3
USADE	Unanticipated Serious Adverse Device Effect	See section 14.3
VAS	Visual Analogue Scale	

> SIGNATURE PAGE

All parties declare by their signature on the electronic and/or separate signature page to follow the Clinical Investigation Plan CP267 in accordance with the Declaration of Helsinki.

SPONSOR

Coloplast A/S

Holtedam 1

DK - 3050 Humlebæk

Denmark

+45 4911 1111

1. List of personnel involved in the investigation

1.1. Sponsor representatives

Sponsor – Coloplast, Medical Affairs.

COORDINATING CLINICAL TRIAL MANAGER	SENIOR STATISTICIAN
[redacted]	

In case of emergency, please contact the CM from the above list of sponsor representatives.

1.2 Investigators

PRINCIPAL INVESTIGATOR & MEDICAL ADVISOR	INVESTIGATOR REPRESENTATIVE
[redacted]	

2. Identification and description of the investigational material

The study includes a range of different adhesive strips with different water absorption properties.

Adhesive strips are not considered medical devices and therefore, approval of the clinical investigation from the competent authorities is not deemed necessary.

3. Justification for conducting the clinical investigation

The adhesives in the ostomy baseplates are developed to make the ostomy product seal to the skin and thereby minimise the risk of leakage episodes.

The purpose of the study is to investigate and understand how different water absorption properties in adhesives affect the initial adhesion and the adhesion during use to human skin.

The data from the investigation will be used to optimize the water absorption properties in adhesives to be implemented in future ostomy products.

Furthermore, data from abdominal skin and peristomal skin are compared to explore the resemblance between the two skin types. This will provide valuable knowledge for the development of ostomy products/adhesives and may minimize the number of clinical studies in ostomy users in the early development phase.

4. Ethical considerations, investigational material and clinical investigation risks and benefits

The clinical investigation is conducted in accordance with current law and applicable standards see section 12.

The rights, safety and well-being of human subjects shall prevail over interest of science and society.

4.1. Anticipated benefits

There is no immediate benefit by participating in the study, however participating subjects will contribute with important information for developing new ostomy products that may reduce skin damage caused by leakage.

4.2. Anticipated risk, side effects and disadvantages

Part A of the study includes healthy volunteers and Coloplast employees. Previous, investigations have been conducted where the participants were Coloplast employees (e.g. journal No 2004-1-47G) and among especially development engineers, there is a wish to participate in the product development/adhesive development as they can obtain valuable knowledge on how it feels to apply, wear and remove adhesives and thereby use this knowledge to the development of the optimal adhesive for ostomy users. Furthermore, this investigation includes only objective endpoint measurements and therefore, it is considered acceptable to include employees. Employees are seen as a vulnerable group and therefore, recruitment and the informed consent procedure are focusing on voluntariness – and will comply with Helsinki declaration which describes that in such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

There are no anticipated high risks during this clinical investigation. However, when performing the peel force of the skin the risk of mild to moderate skin irritation exists.

5. Objectives and hypotheses of the clinical investigation

5.1. Objectives

The primary objective is to investigate water absorption in different adhesives.

Secondary objectives are

- To investigate the impact that different water absorption properties in adhesives have on the initial adhesion, adherent area and skin when applied to skin exposed to buffer, output (simulated in part A and real/simulated output in part B of the study) as well as to dry skin.
- To investigate the impact that different water absorption properties in adhesives have on the adhesion during use with and without conducting exercise (part A and B).
- To explore the variations of adhesive properties when applied to peristomal skin and abdominal skin (part B)
- To explore the variations in water loss and hydration between peristomal skin and abdominal skin (part B)

5.2. Risks and anticipated adverse device effects to be assessed

There are no specific risks or anticipated adverse events to be assessed in this clinical investigation. However, when performing the peel force of the skin the risk of mild to moderate skin irritation exists.

6. Design of the clinical investigation

6.1. General

The investigation is open-labelled and is divided into two parts: Part A evaluates the adhesive strips on abdominal skin in healthy volunteers while part B evaluates the adhesive strips on peristomal and abdominal skin in people with a stoma.

Part A:

Investigation of adhesive strips will be performed in cohorts of minimum 4 and up to 80 subjects. Each cohort consist of 1 or more test visits and a compliance visit. The purpose of the investigation for the individual cohorts will be described in a sub-investigation document.

At each of the test visits, subjects have a maximum of six adhesive strips placed on the skin as illustrated in Figure 1. The adhesive strips are placed on either dry skin or skin wetted by buffer or simulated output. The adhesive strips can be removed at different time slots but after 72 hours at the latest (e.g. after 10, 60 minutes and 24 hours) or within the same time slot.

The ordering of the timeslots position (T1, T2 and T3) from belly - button will be randomized within each cohort if applicable.

Subjects can be asked to take a shower or ride an exercise bicycle for max 1 hour before application of adhesive strips or during wear.

Subjects can also be asked to apply and change adhesive strips every 24 hours between visits but for a maximum of 10 days between two visits. The strips should be applied at the same place every time

Each adhesive strip will be evaluated in a cohort of minimum 4 subjects and up to 80 subjects are enrolled and can test maximum 30 different types of adhesive strips.

Example illustrating test of adhesive strips. T1, T2 and T3 indicates different time slots for removing adhesive strips e.g. 10, 60 minutes and 24 hours:

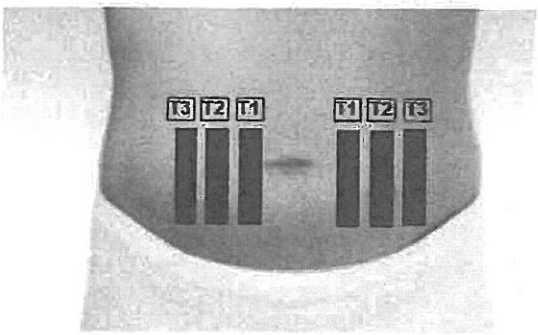


Figure 1

Part B:

At each of the test visits, subjects have a maximum of four adhesive strips placed on the skin as illustrated in the Figure 2. The adhesive strips are placed on either dry skin or skin wetted by buffer, real or simulated output. The adhesive strips will be removed at different time slots but after 72 hours at the latest.

Subjects can be asked to take a shower or ride an exercise bicycle for max 1 hour before application of adhesive strips or during wear.

Subjects can also be asked to apply and change adhesive strips in the abdominal area every 24 hours between visits but for a maximum of 10 days between two visits. The strips should be applied at the same place every time.

Each adhesive strip will be evaluated in a cohort of minimum 4 subjects and up to 50 subjects are enrolled and can test maximum 30 different types of adhesive strips.

The ordering of the timeslots position (T1 and T2) from belly-button will be randomized within each cohort if applicable.

Example illustrating test of adhesive strip. T1 and T2 indicates different time slots for removing adhesive strips e.g. 1 and 24 hours:

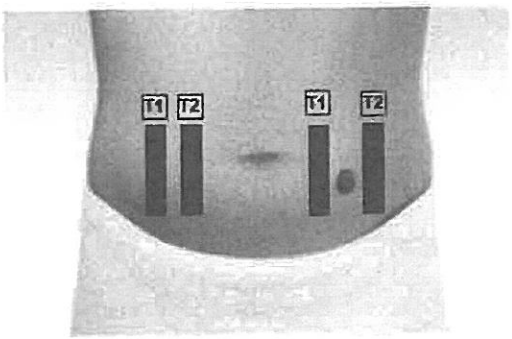


Figure 2.

6.1.1. Primary end point

Primary endpoint:

1. Swelling of adhesive strips measured by weight (Difference between weight of strip before and after test)

6.1.2. Secondary end points

Secondary endpoints:

2. Peel force needed to peel off adhesive strip (assessed when possible)
3. Adherent area on adhesive strip assessed by photos and measured by area (cm^2) or ordinal point scale ranging from very small to very large.
4. Trans Epidermal Water Loss (TEWL)
5. Hydration measured by conductance
6. Redness of skin (erythema) assessed by spectrophotometric method, thermography, photos and potential video sequences
7. pH of skin
8. Discomfort when adhesive strip is peeled off evaluated by the Visual Analogue Scale (VAS) and discomfort during use of adhesive strips evaluated by following questions: 1) Have you experienced any redness under the adhesive? 2) Have you experienced any itching or burning under the adhesive? 3) Do you experience any weeping or moisture on the skin under the adhesive? 4) Have you experienced any pain under the adhesive? 5) Do you experience any bleeding from the skin under the adhesive? The severity of redness, itching and burning, weeping and moisture, pain and bleeding will be rated as None of the time, A little of the time, Some of the time, A lot of the time or All of the time.
9. Adverse events

TEWL, hydration, occurrence of erythema and pH of the skin are measured by three repeated measurements.

Baseline data:

Age
Gender
Height/weight
Informed Consent

For Part B the following will be included as well:

Year of stoma

Type of stoma

Reason for stoma

Leakage pattern

Experiences with moisture and product performance (e.g. skin maceration, leaks after physical activities etc.) – Answer is a comment field

6.1.3. Rationale for the selection and measurement of end points

Peel force: Peel force is a very frequently used and relevant method for recording adhesive properties of new developed skin adhesives. It describes how good the adhesives stick to the skin. [2, 3]. Peel force is measured by peeling the adhesive strips from the skin surface

Adherent area: After peeling the adhesive strips from the skin surface a picture of the adhesives is taken. Based on visual inspection from the picture, the area not affected by water or output is considered the adherent area, which is a measurement for adhesives ability to resist moisture and output. The adherent area is measured by a ruler/ordinal 5-point scale.

Swelling of adhesives strips: The swelling of the adhesive strips measured by the difference in weight before and after test is an indicator of the ability of the amount of moist that the adhesive strips can absorb.

Trans Epidermal Water Loss (TEWL): TEWL is a standardized non-invasively method for describing the barrier function of the skin [1]. Damage to the skin surface (stratum corneum) will lower the barrier of the skin and thereby increase the water loss. This can be used as a proxy for the damaging effects of the adhesive.

TEWL is measured by applying a probe to the surface of the skin. The instrument is a Dermalab (Cortex Technology A/S, Hadsund).

Skin Conductance and Capacitance (hydration): Conductance and Capacitance is standardized non-invasively methods for measuring the hydration of the skin [1]. Both the conductance and capacitance is proportional to the skins hydration state and how the skin is influenced by adhesives. The capacitance measurement can measure deeper in the skin whereas the conductance measures in the top layer of the skin. Both measurements are done by applying a probe to the surface of the skin. The instruments is either a DermaLab (conductance, Cortex Technology A/S, Hadsund) or a MoistureMeterD (capacitance, Delphin Technology).

Occurrence of erythema: A change in the surface skin color is known to be related to a change in the blood flow. This can be measured non-invasively with a spectrophotometric instrument (Dermaspectrophotometer, Cortex Technology A/S, Hadsund) where both the redness and the color of the skin are measured.

pH: How the skin PH is influenced by adhesives. (applying a probe to the surface of the skin)

Discomfort: The VAS is an instrument used to subjectively evaluate the discomfort when the strip is peeled off. The subject will be asked to mark the evaluation as a vertical line on the 10 cm horizontal VAS ranging from "no discomfort" to "worst possible discomfort" caused when the strip is peeled off. Discomfort during use

of adhesive strips evaluated by questions regarding subject experience in redness under the adhesive, feeling of itching and burning under the adhesive, weeping or moisture under the adhesive, pain and bleeding from the skin.

User experience is a very important part of product development in Coloplast A/S and the selected questions relate to how the adhesive strips affects the skin.

Adverse Events: All adverse Events are captured and documented throughout the study.

6.1.4. Discussion of the clinical investigation design

Up to 130 subjects will be enrolled in total; up to 80 healthy volunteers will be enrolled in part A and up to 50 with a stoma will be enrolled in part B.

To be included in the investigation, the subjects must comply with the selection criteria described in section 6.1.5 and must not comply with criteria described 6.1.5.

6.1.5. Inclusion and Exclusion criteria for subject selection and justification

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

Part A:

Inclusion criteria:

1. Have given written informed consent

2. Be at least 18 years of age and have full legal capacity

3. Have intact skin on the area used in the investigation

Exclusion criteria

5. Currently receiving or have within the past 2 months received radio- and/or chemotherapy
6. Currently receiving or have within the past months received topical steroid treatment in the abdominal skin area or systemic steroid (tablet/injection) treatment.
7. Are pregnant or breastfeeding
8. Have dermatological problems in the abdominal area (assessed by investigator)

Part B

Inclusion criteria:

1. Have given written informed consent

2. Be at least 18 years of age and have full legal capacity

3. Have had a stoma for more than one year

4. Has an ostomy with a diameter up to 35 mm

5. Have intact skin on the area used in the investigation

Exclusion criteria

1. Currently receiving or have within the past 2 months received radio- and/or chemotherapy

2. Currently receiving or have within the past month received topical steroid treatment in the peristomal skin area or systemic steroid (tablet/injection) treatment.

3. Are pregnant or breastfeeding

4. Have dermatological problems in the area used in the investigation (assessed by investigator)

Part A

Justification for inclusion criteria:

1. To meet the Helsinki Declaration

2. To meet the Helsinki Declaration

3. The adhesive strips must be applied on intact skin

Justification for exclusion criteria:

1. The skin undergoes major changes as a consequence of radio- and/or chemotherapy, and therefore it can be more fragile

2. Steroid product may interfere with the study endpoints by making the abdominal skin thinner and more fragile

3. Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, foetuses and infants are unknown

4. The skin has to be intact in order to see a potential damage of the skin with the simulated output

Part B

Justification for inclusion criteria:

1. To meet the Helsinki Declaration

2. To meet the Helsinki Declaration

3. To ensure subjects are recovered from ostomy surgery

4. To be able to have adhesive strips applied to the peristomal area

5. The adhesive strips must be applied on intact skin

Justification for exclusion criteria:

1. The skin undergoes major changes as a consequence of radio- and/or chemotherapy, and therefore it can be more fragile to baseplate changes

2. Steroid product may interfere with the investigational endpoints by making the peristomal skin thinner and more fragile

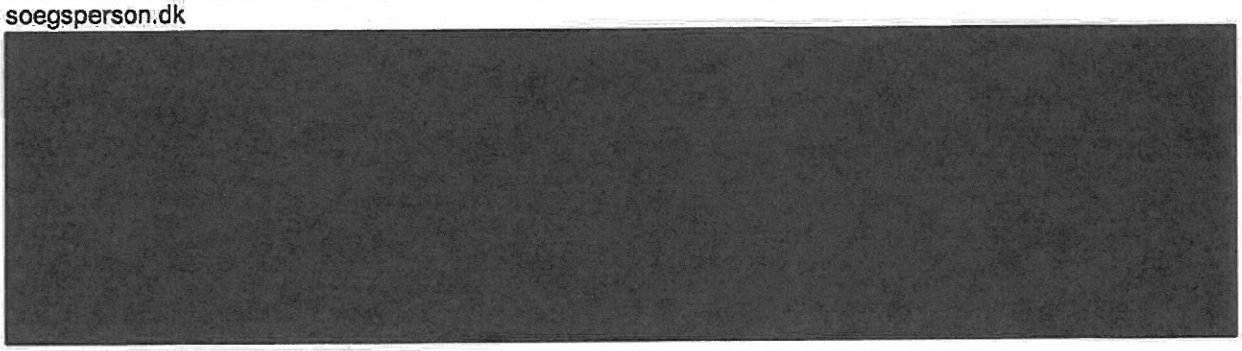
3. Even though the ingredients and the recipes have been approved for human beings, their effect on embryos, foetuses and infants are unknown

4. The skin has to be intact in order to see a potential damage of the skin with simulated /real output

5. Other interventional investigation guidelines/products may interfere with these investigational endpoints.

6.1.6. Recruitment and enrolment

Part A of the study includes healthy volunteers and employees from Coloplast A/S. Previously , investigations have been conducted where the participants were employees (e.g. journal No 2004-1-47G) and among especially development engineers, there is a wish to participate in the product development/adhesive development as they can obtain valuable knowledge on how it feels to apply, wear and remove adhesives and thereby use this knowledge for the development of the optimal adhesive for ostomy users. Furthermore, this investigation includes only objective endpoint measurements and therefore, it is considered acceptable to include employees. Employees are seen as a vulnerable group and therefore, recruitment and the informed consent procedure are focusing on voluntariness. The informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship. The Clinical Manager will perform recruitment through advertisement and posters on the Coloplast location at Holtedam 3, DK-3050 Humlebæk and on Forsoegsperson.dk



The recruitment of potential subjects will commence only once authorisation has been received from Ethics Committee.

If a potential subject is interested in participating, then written information about the investigation (subject information) will be sent to the subject to ensure that potential subjects are given the opportunity to read about the investigation before a possible informational visit, and so that they can prepare any possible questions they may have. The subject information provides information to potential subjects about how to contact the investigator or a representative thereof, or a representative of the sponsor (name, telephone number and e-mail address), if they wish to learn more about the study.

If the potential subject is interested in participating in the investigation, a visit will be arranged in a room reserved for the purpose of ensuring privacy and quiet surroundings at Coloplast. The subjects will receive both written and verbal information about the possibility of bringing a companion to the informational visit and to any possible subsequent visits. See section 13 for information to be given to the subjects, as well as the informed consent process.

6.1.7. Subject withdrawal criteria

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

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

- Non-compliance with the CIP affecting the scientific integrity of the investigation.
- If a subject's safety and well-being is compromised by further participation.
- If it becomes apparent or circumstances change so, a subject do not comply with one or more of the selection criteria.

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 14.

6.1.8. Point of enrolment

A subject is considered enrolled in the investigation when written informed consent is obtained and the subject has been randomised to a 'treatment' sequence. The expected duration of involvement for each subject is described in section 6.2.1.

6.1.9. 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. The relevant EC will be notified of changes. The investigation is terminated when the last subject has ended his/her participation.

- First subject enrolled (May/2016).
- Last subject completed (June 2021).

6.1.10. Total number of subjects

Up to 130 subjects will be enrolled in total; up to 80 healthy volunteers will be enrolled in part A and up to 50 subjects with a stoma will be enrolled in part B.

For further information on the number of subjects to be enrolled please refer to the sample size calculation in section 7.2. If the expected number of subjects is not reached within the timelines, the recruitment can be prolonged.

6.2. Procedures

6.2.1. Clinical investigation-related procedures

Before initiation of the clinical investigation, the sponsor must be provided with key investigational personnel's current signed and dated CVs to verify their qualifications. Key site personnel are those who treat or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all site personnel are trained in the investigation procedures, how to complete the CRFs, the procedure for reporting an adverse event or serious adverse event (how, when, to whom), and who to contact in the case of an emergency related to the investigational device.

Inclusion visit:

- Introduction to the study
- Inclusion in study
- Baseline information is obtained
- Instruct subject to pre-strip of abdominal skin

Test visits 1-25 (up to maximum 25 visits per subject. (1-3 days after pre-stripping the abdominal skin):

- Baseline measurements are conducted on both sides of the stomach (TEWL, hydration, erythema, pH – 3 repeated measurements under each adhesive strip area (upper, middle and bottom of adhesive strip)
- Potential wetting of skin - shower/bicycle exercise (max 60 minutes) and after-wetting baseline measurements are conducted (TEWL, hydration, erythema, pH – 3 times/strips (upper, middle and bottom of adhesive strip))
- Adhesive strips are weighted and applied
- Potential shower/bicycle exercise (max 60 minutes)
- Adhesive strips are removed at pre-defined timeslots (peel force measured)
- Discomfort when strip was peeled of is evaluated by subject (VAS) and discomfort during use of strips are evaluated by questions.
- Measurements are conducted (TEWL, hydration, erythema, pH – 3 times/strips (upper, middle and bottom of adhesive strip))
- Acclimatization ½
- Measurements are conducted (TEWL, hydration, erythema, pH – 3 times/strips (upper, middle and bottom of adhesive strip))
- Adhesive strips are weighed
- Photo of adhesive strips

For part A: The subjects can be asked to apply and change strips every 24 hours between two test visits but for a maximum of 10 days between two visits. The strips should be applied at the same place every time

For part B: The subjects can be asked to apply and change strips in the abdominal area every 24 hours between two test visits but for a maximum of 10 days between two visits. The strips should be applied at the same place every time

Compliance visit:

A compliance visit is conducted after each cohort has been performed. (minimum. 3 days after last visit).(this can be done by a phone call).

Termination visit:
A termination visit is conducted when subject terminates the study. (minimum. 3 days after last visit).

If the subject experiences skin complications during the visits the investigator or investigator representatives will evaluate the skin condition in order to decide whether subject can continue the study.

For part B, CE-marked ostomy bags are applied to the ostomy to collect output during the test.

6.2.2. Activities performed by sponsor representatives

The investigation will be conducted at a clinical facility at Coloplast, Holtedam 1, 3050 Humlebæk, Denmark. The Principal Investigator is overall responsible for the investigation. The sponsor representatives will be present at all study activities and all subjects visits.

During the investigation, sponsor's representatives will monitor the investigation closely.

6.2.3. Foreseeable factors that may compromise the outcome/results

There are no known foreseeable factors that may compromise the outcome of this investigation.

6.2.4. Flow chart

Table 1 Chart showing scheduled visits and corresponding assessments.

	PERFORMED BY	INFORMATION MEETING	VISIT 1-25	COMPLI-ANCE/TERMINA-TION VISIT
General *(performed by investigator)*				
Oral information	Independent nurse (part A) Investigator (part B)	X		
Written informed consent	Independent nurse (part A) Investigator (part B)	X		
Randomisation	Investigator		X	
Check of inclusion and exclusion criteria	Investigator	X	X	
Registration of baseline information	Investigator	X		
Registration/measurement of end points				
Stripping abdominal skin*	Subject (1-3 days before each visit)		X	
Apply adhesive strips*	Investigator		X	
Evaluate discomfort (VAS) and discomfort during use of strips evaluated by questions	Subject		X	
Measure peel force, TEWL, hydration, erythema and pH	Investigator		X	
Photo of adhesive strips	Investigator		X	
Registration of termination				
AEs/ADEs/SAEs/SADEs	Investigator		X	X
Compliance form	Investigator			X
Termination form	Investigator			X

*The subjects themselves can be asked to apply and change the strips every 24 hours between visits (for part B only in the abdominal area). In the case hereof the pre-stripping 1-3 days before a visit will not be applicable.

6.2.5. Randomisation procedure

If applicable, randomisation will be performed within each cohort. The investigator/investigator representative will receive sealed envelopes containing consecutive numbers, which indicate the subjects randomisation numbers and test set-up. The randomisation lists are generated using SAS version 9.4 or JMP® version 12. The Randomisation lists are archived in the Sponsor File.

6.2.6. Blinding

This investigation is not blinded.

6.2.7. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully completed in the CRF. The sponsor will provide the CRF for the investigation. Each subject will have a unique subject ID within the investigation. It is the responsibility of the investigator to ensure that all data are completed promptly and correctly.

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

Regarding the endpoint measured by the VAS scale, the subject will fill out these on separate paper sheets for this purpose. After completion, the investigator or relevant staff will measure and complete endpoint in the CRF.

Any corrections in the CRF must be clearly signed and dated by the investigator or relevant staff. The corrected entry must be crossed out so that the original entry is still legible, as shown below:

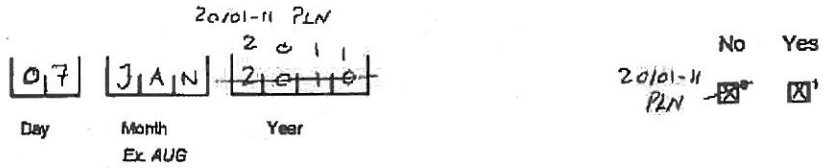


Figure 1: Two examples of how to make corrections in the CRF.

6.2.8. Concomitant treatment

After skin has been pre-stripped, subjects are not allowed to use lotion on the area before the visit days.

6.3. Monitoring plan

During the investigation period, monitoring is carried out by the sponsor. Ongoing monitoring will be performed during the study conduct to ensure the CRFs have been filled in correctly; every second subject will be monitored. Source data such as informed consent will be 100 % verified.

6.3.1. Source data verification

All Informed Consent Forms and CRF`s will be seen as source data. Regarding the endpoint measured by the VAS scale, the paper sheet filled out by the subject will be source data.

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

6.3.2. Other methods for data quality assurance

The sponsor, sponsor's representative and/or investigational sites may be inspected by competent authorities or their representatives and likewise may be audited according to Coloplast's internal quality audit plan and procedures.

7. Statistical considerations

7.1. Statistical design, method and analytical procedures

Each adhesive will be evaluated in a cohort of minimum four subjects. For each cohort primary and secondary endpoints will be summarized and listed. Data will be analysed ongoing by cohort. The results will together with data from laboratory models provide information for further development of adhesives to be tested in the pilot evaluation. A joint evaluation of all adhesives will be performed when all data has been collected. The evaluation will primarily be based on summary statistics for each cohort. Explorative analyses combining data from different cohorts may also be performed.

7.2. Sample size

A minimum of four subjects will be included in each cohort. Up to 130 subjects will be enrolled in total; up to 80 healthy volunteers will be enrolled in part A and up to 50 with a stoma will be enrolled in part B. This is a pilot evaluation of adhesives under development. The evaluation will be supported by data from laboratory models. Four subjects in each cohort is expected to provide enough information for further development of the adhesives. More subjects may however be included in a cohort if deemed necessary.

7.3. Level of significance and power

The data will primarily be evaluated based on summary statistics and listings of data from cohort. If explorative statistical analyses are performed a significance level of 5% will be applied.

7.4. Pass/fail criteria

No formal success criteria are applied in this explorative investigation. The investigation will provide valuable insight into water absorption properties of different adhesives and to which degree these impact the adhesion and skin as well as insights to a potential resemblance between abdominal and peristomal skin.

7.5. Interim analysis

Data will be analysed ongoing by cohort to support the development of additional adhesives to be tested in the investigation. A final reporting will take place when all data is available.

7.6. Statistical reason for termination of investigation

There is no reason to terminate the investigation based on statistical considerations.

7.7. Deviation(s) from the statistical plan

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

8. Data management

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

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

Data will be captured in the iMedidata, Rave system. Data Management is responsible for control of data consistency and also for completeness of data from each subject.

Discrepancies are generated through queries in the Rave data management system. The investigator is responsible for resolving these promptly. When all queries are resolved, the database is locked and the statistical analyses are performed.

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

The Rave EDC version number 2018.2.4 will be used for data management. 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.

8.3. Data retention

The sponsor's file, all investigation site files and the investigation database, must be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

9. Amendments to the Clinical Investigation Plan

Any significant changes to the CIP must be:

- Agreed between the sponsor and PI
- Justified in a statement included in the amended section. The version number and date of amendment must be documented.
- Registered in the Change Log.
- Notified to or approved by the EC before implementation (if applicable).

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

10. Clinical Investigation Plan deviations

The Investigator is not allowed to deviate from the CIP unless under emergency circumstances and to protect the rights, safety and well-being of the subject(s). Deviations must be reported to the sponsor and deviations affecting the scientific aspect of the investigation or the safety of the subject are reported to the EC by the sponsor if required by national regulations.

Definition of deviation:

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

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

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

11. Device accountability

No accountability will be made as no medical devices are being tested.

12. 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 64th WMA General Assembly, Brazil, October 2013.
- The study is conducted as far as possible in compliance with ISO 14155 considering the nature of the study not investigating a medical device
- Act of processing of Personal data Act. no. 429 of 31st May 2000

12.1. Ethics committee

The CIP 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 substantial amendment to the protocol will be submitted to the same EC.

The sponsor will notify the EC regarding the end of the clinical investigation no later than 90 days after the last patient has ended his/her participation.

Adhesive strips are not considered medical devices and therefore, approval of the clinical investigation from the competent authorities is not deemed necessary.

12.2. Other relevant authorities

Coloplast follows Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data

12.3. Data protection

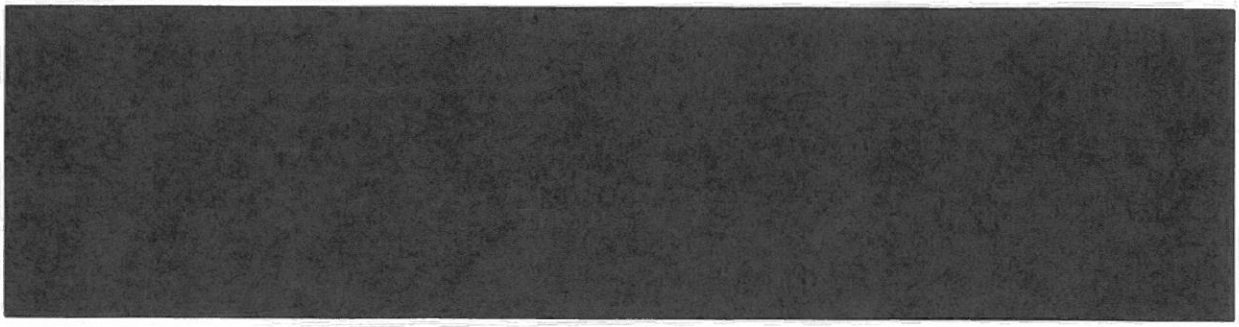
Information about the subject's identity is filed as a confidential document by the investigator(s) and subjects are referred to only as numbers on all other documents. The data are blinded correspondingly in the data analysis.

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

12.4. Indemnity

In case of damage as a result of this test the subject are not covered by the general patient compensation system, but covered by the common policies by Danish law concerning compensation. Additionally healthy trial participants are also covered by workers' compensation law. If the participation in the trial is the cause of personal injury, the participant will also be covered by Coloplast's product liability insurance.

12.5. Financial conditions



13. Informed consent process

Written informed consent is obtained from all subjects participating in the investigation following detailed written and verbal briefing. An independent study nurse in part A of the study (not employed at Coloplast) and the investigator, or his/her representative in part B of the study, provides a non-technical version of this information to the subject in their native language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks or inconveniences and/or expected benefits. Subjects will have time to ask questions and have a minimum of 24 hours before deciding on whether or not to participate in the investigation. Subjects will be informed that their participation is voluntary and that they may leave the investigation at any time, without influencing their further treatment.

The informed consent signature form includes the signatures of the subject and the independent nurse/PI, or his/her representative who is responsible for conducting the informed consent process, which are dated in person. A copy will be provided to the subject.

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

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

For participants, who are not an employee at Coloplast: Confidentiality Agreement between the participant in the study and Coloplast:

Coloplast, wish to involve the user in testing of improved ostomy products as early as possible. In order to obtain a good product it is essential for us to get the user's wishes and comments to the new products as early as possible.

Further, it is important for Coloplast to ensure that any new inventions can be patented. To obtain a balance between involving the user at a very early stage and at the same time not waive our rights, we have chosen to ask the participants to treat the products and the material they receive from Coloplast in a confidential way.

The confidentiality only concerns the physical materials and products, which are delivered by Coloplast and it does not in any way influence other aspects of the user's rights.

The primary purpose of the confidentiality is to ensure that a possible breach of contract will fall under the Danish Patent Act §2(2) and thereby ensure that Coloplast still has the possibility to obtain a patent, and for Coloplast it is not common practice to initiate court cases on the basis of any minor breach of contract.

14. Adverse events, serious adverse events and device deficiencies

14.1.1. Adverse event (AE)

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical sign (including abnormal laboratory findings) that may occur in subjects, users or other parties, whether or not it is related to the medical device(s), or the procedures involved. This could include events such as headache or dizziness.

14.1.2. Adverse device effect (ADE)

(Although not testing medical device the term device is still used in this section.) An adverse event, which is related to the use of the investigational medical device, is an adverse device effect, and should be marked as related or possibly related to the medical device(s) on the adverse event form.

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

Table 2 lists anticipated adverse device effects that may occur.

Table 2 Anticipated adverse device effects and their likely frequency rates

ANTICIPATED ADE
Peristomal skin irritation
Mechanical Trauma

Temporary redness upon removal of the base plate is not considered to be an ADE. However, an abnormal development in the intensity or duration of redness should be considered an ADE.

14.2. Device deficiency

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

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

14.3. Serious adverse events

14.3.1. Serious adverse event (SAE)

A serious adverse event is an adverse event that:

- Led to death.
- Led to a serious deterioration in the health of the subject that either resulted in:
  1) a life-threatening illness or injury, or
  2) a permanent impairment of a body structure or a body function, or
  3) required inpatient hospitalisation or prolongation of existing hospitalisation, or
  4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or function.

- Led to fetal distress, fetal death or a congenital abnormality or birth defect.

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

- Suitable action had not been taken, or
- Intervention had not been made, or
- Circumstances had been less fortunate.

These are handled under serious adverse event reporting.

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

14.3.2. 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.

14.3.3. Anticipated serious adverse device effect (ASADE)

An anticipated serious adverse device effect is any event that by its nature, incidence, severity or outcome has previously been identified in the risk analysis report.

14.3.4. 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.

14.4. Medical care of subjects

The PI will ensure that adequate medical care is provided to any subjects experiencing an adverse event during or after participation in the clinical investigation, if the investigator is familiar with the event and the event might have occurred on the basis of this investigation. All serious adverse events will be followed until a resolution is addressed.

The current status of all ongoing adverse events is documented during site close-out.

14.5. Reporting and timelines

14.5.1. Investigator's reporting responsibilities

- All serious adverse events and serious adverse device effects must be reported to the sponsor within 24 hours of the site personnel becoming aware of the event.
- A device deficiency that could have led to a serious adverse event but did not do so because suitable action was taken, intervention had been made or because of fortunate circumstances should be reported to the sponsor within 24 hours of the site personnel becoming aware of the event.
- New findings and/or updates in relation to already reported serious adverse events should also be reported to the sponsor within 24 hours of the site personnel becoming aware of the event.
- Device deficiencies and all adverse device effects must be reported by the monitor to the sponsor in the periodic site monitoring report.

All the serious adverse events listed above must be reported using the relevant adverse event/serious adverse event/device deficiency form.

Please report to:

[redacted]

14.5.2. Sponsor's reporting responsibilities

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

- 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 related to such a serious adverse event, the sponsor must immediately, but no later than 2 calendar days after they are made aware of the event, report it to national regulatory authorities.

15. Suspension or premature termination of the clinical investigation

The sponsor may suspend or prematurely terminate an investigation site or the entire clinical investigation for significant and documented reasons.

If a suspicion relating to an unacceptable risk to subjects arises during the clinical investigation, the sponsor will suspend the investigation if the risk cannot be assessed immediately. The sponsor will terminate the investigation if an unacceptable risk is confirmed.

The sponsor must ensure that the ethical committees that are considering or have approved the investigation are promptly informed of any suspension or premature termination of the investigation. (In DK the time line for reporting to EC is no more than 15 days)

If monitoring or auditing of the clinical investigation identifies serious or repeated deviations at one of the participating investigation sites, the sponsor will suspend or terminate the particular investigation site. The sponsor will inform the EC about the termination of the site.

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

16. Clinical investigation report

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

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

The clinical investigation report must be submitted to the relevant EC - in DK it must be submitted within 1 year after LPO).

17. Publication policy

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

The investigation will be registered on a public accessible database before recruitment of the first subject. The results of the investigation, positive as well as inconclusive and negative will be published in the same public accessible database (www.clinilcaltrials.gov) Part A and Part B will be published separately in the database. Each cohort will be published separately in the database. The subjects' identity will remain confidential. Whether the results will be submitted to a scientific journal or to conferences is not decided yet. Publication of results in the database will be initiated as soon as scientifically acceptable and according to the law of personal data protection, however within one year after the last subject has completed the investigation.

- Data from the investigation is considered confidential until it is published according to the conditions of this CIP and the 'Clinical Publication Policy'.
- Sponsor may publish anonymous single subject case stories (or public, if the subject consent) at any time during and after the investigation.
- Sponsor reserves the right to use the data (published and unpublished) for reimbursement or regulatory purposes.

18. Bibliography

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[2] Fumio T, Yumi Y, Takeyasu H, Hiroshi N. Regional differences in adhesive tape stripping of human skin, Skin Research and Technology 2006; 12: 178–182

[3] Karwoski AC, Plaut RH. Experiments on peeling adhesive tapes from human forearms, Skin Research and Technology 2004; 10: 271–277