Statistical Analysis Plan (SAP)

Sponsor:	Essity Hygiene and Health AB
Study code:	POWER (NCT04846270)
Study title:	An open, single-arm, post-market clinical investigation to verify the ability of TENA SmartCare Change Indicator™ to reduce the number of manual checks between changes of absorbing incontinence products in a home environment.
Version and Date:	Version 2.0, 25-Nov-2021

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1 LIST OF ABBREVIATIONS

ADE – Adverse Device Effect
AE – Adverse Event
ASADE – Anticipated Serious Adverse Device Effect
CER – Clinical Evaluation Report
CF – Clean File
CI – Confidence Interval
CIP – Clinical Investigational Plan
CRF – Case Report Form
DEU – Dependent End User, synonymous with “subject”
FAS – Full Analysis Set
GLOBIAD – Ghent Global IAD Categorisation Tool
IAD – Incontinence associated dermatitis
PPS – Per Protocol Set
SADE – Serious Adverse Device Effect
SAE – Serious Adverse Event
SAF – Safety Analysis Set
SAP – Statistical Analysis Plan
SAS – Statistical Analysis System
UI – Urinary Incontinence
USADE – Unanticipated Serious Adverse Device Effect
WHO – World Health Organisation

2 INTRODUCTION

This Statistical Analysis Plan (SAP) gives details regarding the statistical analyses and data presentation outlined in the final Clinical Investigation Plan (CIP), version A, 07-Sep-2020 for the POWER study (Ref 1.). Any changes from the final CIP are given in Section 8.

3 CLINICAL INVESTIGATION DETAILS

3.1 Clinical Investigation Objectives

3.1.1 Primary objective

To demonstrate performance through the ability to reduce the number of manual checks in-between changes of absorbing incontinence products using the TENA SmartCare Change Indicator compared to Standard of Care.

3.1.2 Secondary objectives

- Evaluate safety through analyzing device-related adverse events reported during the investigation.
- Evaluate leakage into clothes and/or bed linen.
- Evaluate change in skin redness and irritation.
- Evaluate usability
- Evaluate the number of fecal incidences

3.2 Clinical Investigation Design

This is a prospective, interventional, post-market clinical investigation with the aim to demonstrate the performance and safety of the TENA SmartCare Change Indicator when used as intended in subjects affected with Urinary Incontinence (UI) compared to Standard of Care. The outcome will be evaluated and incorporated in the device specific Clinical Evaluation Report (CER) and serve as a base for continuous investigations.

Thirty-five (35) Dependent End Users (DEUs) with UI cared for in a home environment mainly by one Care Giving Relative (CGR) will be recruited in Poland.

The clinical investigation is designed to be conducted in the individuals home environment, for a duration of three (3) weeks + potential incontinence product training week (one) and potential additional days depending on the visit window scheduling. Eight visits are planned for each subject during the duration of the clinical investigation. However, two of the visits are optional and conducted as needed. If considered necessary by the investigator, nurse, or CGR, additional contacts (e.g. visits/phone calls/video calls) can be arranged. The first week will establish an individual baseline for each DEU, during which the number of manual daily checks between changes of the TENA incontinence product are to be registered by the CGR. During the second week the CGR will be provided the TENA SmartCare Change Indicator and learn how to set up and use it as intended by the manufacturer. During the third week the TENA SmartCare Change Indicator will be used as intended by the manufacturer, while the number of additional manual checks between changes of the TENA incontinence product are to be registered by the CGR. The number of manual checks will be analyzed with regard to the individual baseline in order to evaluate the reduction of manual checks.

The overall duration of the investigation is estimated to 8 months, including a 6-month recruitment period. Expected duration of each subject's participation is 3-6 weeks depending on potential incontinence product training week and potential additional days depending on the visit window scheduling.

3.3 Number of Subjects

The aim is to enroll 35 subjects including a 30% drop-out rate.

3.4 Methods of Assigning Subject to Device Groups

POWER is a post-market, single arm investigation with no planned subgroups analyses.
Each participating subject will be provided with the study device; TENA SmartCare Change Indicator (sensor and app).
The DEU will act as its own control and documented checks during the investigational week will be compared to the Standard of Care during the baseline week.

3.5 Blinding

Not applicable, as this is a non-randomized single-arm clinical investigation.

4 STATISTICAL AND ANALYTICAL PLANS

If nothing else is stated, descriptive statistics will be given for each variable in the trial. This means number of subjects (n), mean, median, standard deviation (SD), minimum (min) and maximum (max) values will be presented for continuous data and frequencies and percentages for categorical data.

All output from the statistical analysis plan will be part of the Clinical Investigation Report (CIR).

4.1 Sample Size Justification

The sample size calculation is based on the assumption of a reduction of the number of manual checks in-between incontinence product changes by 30%. Based on data from SCA and Ipsos MORI Care Giving Relatives Research - Internal and Client Use (Ref 2.) and the statistical power in section 4.5 this give a sample size of 24 subjects. Assuming a 30% dropout rate, the investigation will include up to 35 subjects. If for any reason the dropout rate should be higher than this, additional subjects might be enrolled in the investigation to reach a total of 24 completed subjects.

4.2 Definition of Analysis Sets

The analysis sets described below will be used for the statistical analysis and presentation of data.

4.2.1 Safety Analysis Set (SAF)

The SAF will consist of all consented subjects.

4.2.2 Full Analysis Set (FAS)

The FAS will include all subjects included in the SAF and have at least one set of efficacy measurements after using the investigational device.

4.2.3 Per Protocol Set (PPS)

The PPS will include all subjects included in the FAS who:

- Do not have any other major CIP deviations, which will affect the assessment of efficacy.

The final criteria for the PPS, regarding which CIP deviations that warrant exclusions, will be determined when all data on CIP deviations are available and before any statistical analysis has taken place.

4.2.4 Use of Analysis Sets

The presentation of safety data will be based on the SAF.
The presentation of baseline characteristics and demographics will be based on the FAS.

The primary endpoint analysis will be performed using both the FAS and the PPS. The FAS will be considered as the main analysis.

4.3 Definition of Baseline

The first week will establish an individual baseline for each DEU, during which the number of manual checks between changes of the TENA incontinence product are to be registered continuously in a diary by the CGR.

4.4 Summary Statistics

In general, all data collected will be presented with summary statistics and given in patient data listings (an overview of patient data listings are given in Section 9). Summary statistics will include number of patients, mean, standard deviation, median, minimum and maximum for continuous data and frequency and percentage for categorical data.

4.5 Significance Level and Power

All statistical testing will be performed at the 5% significance level. The level of statistical power is set to 90% for the primary endpoint.

4.6 Multiple Comparisons/Multiplicity

No adjustment for multiplicity of testing will be done. There will be one formal statistical analysis (primary efficacy endpoint) in line with the sample size determination. All other statistical tests will be considered as descriptive.

4.7 Handling of Drop-outs, Missing Data and Outliers

Outliers will be included in summary tables and listings, and will not be handled separately. Available data from prematurely withdrawn subjects will be included in the analysis as far as possible. Missing data will not be imputed.

4.8 Adjustment for Covariates

Not applicable.

4.9 Multicenter Studies

Not applicable.

4.10 Examination of Subgroups

No examination of subgroups is planned.

4.11 Blind Review

Not applicable, as this is a non-randomized single-arm clinical investigation.

5 SUBJECTS

5.1 Subject Disposition

The number of subjects that entered the study, withdrawn subjects, completed subjects and the number of subjects at each visit will be summarized.

5.2 Baseline Characteristics and Demographics

The following baseline characteristics will be given in total:

- Age
- Gender
- Evaluation of general cognitive function
- Ghent Global IAD Categorisation Tool - GLOBIAD score

Medical history, physical examination, concomitant medication, urine pregnancy test collected at visit 1 (screening) will be listed only.

6 TREATMENT INFORMATION AND EXTENT OF EXPOSURE

6.1 Active Treatment

Active treatment in this study is the use of TENA SmartCare Change Indicator (sensor and app).

6.2 Placebo Treatment

Not applicable as no placebo treatment is involved.

6.3 Extent of Exposure

The exposure of study devices for each subject is estimated to 2 weeks.

6.4 Compliance of Study Device

Compliance of the study device will be determined by observing that the devices are being used as is registered in the device system.

6.5 Concomitant Medications

Subjects are allowed to continue their regular medication during the study. Relevant concomitant medication data will be listed only.

7 STATISTICAL METHODOLOGY

All efficacy parameters will be presented using summary statistics. Additional statistical analyses are specified below.

7.1 Primary efficacy endpoint

7.1.1 Definition

The primary efficacy endpoint is the change in percentage of the number of manual checks between week 1 and week 3 of the investigation. The average manual checks/day for a subject week will be used for the percentage calculation, since data may be available for less or more than 7 days.

7.1.2 Analysis

A one-tailed paired t-test will be used to test if the number of manual checks has been reduced relative to week 1. If the variable is not normally distributed the non-parametric Wilcoxon signed-rank test will be used and in case of a significant result, a one-sided 95% confidence interval will be constructed for the percentage change in checks between week 1 and week 3 to validate at least a 30% reduction. The Shapiro-Wilk test will be used to test normality.

7.2 Secondary Efficacy Endpoints

- Change in the number of leakages into the clothes and/or bed linen at week 3 (investigational week) compared to week 1 (baseline week).

  A paired t-test will be used for comparison. If the variable is not normally distributed a non-parametric Wilcoxon signed rank test will be used.

- Evaluate change in skin redness and irritation, at week 3 (investigational week) compared to week 1 (baseline week).

  This endpoint will be evaluated using the Ghent Global IAD Categorisation Tool (GLOBIAD) (Ref 3.). GLOBIAD is a categorisation tool to monitor Incontinence associated dermatitis (IAD) prevalence and incidence. IADs can be scored as 1A, 1B, 2A and 2B. The analysis is to determine if there is a significant difference in scoring between the two time points. A paired t-test will be used for comparison. If the variable is not normally distributed a non-parametric Wilcoxon signed rank test will be used.

- Evaluate the number of fecal incidences.

A non-parametric Wilcoxon signed rank test will be used for comparison.

- Evaluate usability
  Descriptive and summary statistics

The Shapiro-Wilk test will be used to test normality where appropriate.

7.3 Secondary Endpoint / Safety Endpoint

Incidence of adverse events and device deficiencies; AEs, ADEs, SAEs, SADEs and DDs.

7.3.1 Definitions

For full details on AEs, Adverse Device Effects (ADEs), Serious Adverse Events (SAEs), Serious Adverse Device Effects (SADEs) and Unanticipated Serious Adverse Device Effect (USADE) please refer to the CIP.

Adverse Event (AE)
Untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated

Note 1: This definition includes events related to the investigational medical device or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices.

Adverse Device Effect (ADE)
Adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Note 3: This includes comparator if the comparator is a medical device.

Serious Adverse Event (SAE)
Adverse event that led to any of the following:
a) death,
b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
   - a life-threatening illness or injury, or
   - a permanent impairment of a body structure or a body function including chronic diseases, or
   - in-patient or prolonged hospitalization, or
   - medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,

c) foetal distress, foetal death, congenital abnormality, or birth defect including physical or mental impairment.

Note 1: 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.

Serious Adverse Device Effect (SADE)
Adverse device effect that has resulted in any of the consequences characteristic of a SAE.

Unanticipated Serious Adverse Device Effect (USADE)
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.

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

7.3.2 Analyses

No statistical analyses are planned for safety parameters. The safety endpoint will be summarized using descriptive statistics.

7.3.3 Presentation

AE/ADE:
The following summaries of AEs and SAEs will be given:

- Total number of AEs
- Total number of unique AEs
- Total number of unique, related AEs
- Total number (%) of subjects with at least one AE
- Total number (%) of subjects with at least one related AE
- Total number (%) which had AE as reason for premature discontinuation of study device

Severity, action taken, concomitant therapy started and subject outcome of the AEs will be given in data listings only. AEs, which were reason for premature discontinuation of study device, will be listed separately.

Depending on the number of AEs reported, the most frequently reported (e.g. in more than 5% of the patients) AEs might be summarized separately.

The total number of SAEs and patients with a least one SAE will always be given. Further summaries of SAEs depending on the number of SAEs observed.

SAE/SADE:
SAEs/SADEs, if any, will be listed only.

7.4 Interim Analysis

Not applicable. No interim analysis planned.

8 CHANGES FROM THE CIP

Not applicable, no changes made.

9 STATISTICAL DELIVERABLES

The following documents will be delivered:

- Statistical Analysis Plan (SAP)
- Statistical analyses and summary tables
- Appendices with patient data listings:
  - Discontinued patients
  - CIP deviations
  - Patients excluded from the efficacy analysis
  - Demographic
  - Exposure to study device
  - Adverse event

10 SOFTWARE

All statistical analyses will be performed using SAS Version 9.4 (SAS institute, Cary, NC).

11 REFERENCES

Ref 1. POWER Clinical Investigation Plan, version A, 07-Sep-2020
Ref 2. SCA and Ipsos MORI Care Giving Relatives Research - Internal and Client Use - 30.10.17 – v1
Ref 3. The Ghent Global IAD Categorisation Tool (GLOBIAD) 2017, Skin Integrity Research Group-Ghent University. www.UCVVGent.be.

12 APPROVAL

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