essity	Cover page – Statistical Analysis Plan (SAP)

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An explorative, open, single-arm clinical investigation to collect real-life measurement data in order to assess the mathematical algorithms involved in TENA SmartCare Change Indicator.

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CONFIDENTIAL

Statistical Analysis Plan (SAP)

Sponsor:	Essity Hygiene and Health AB
Study code:	FUEL
Study title:	An explorative, open, single-arm clinical investigation to collect real-life measurement data in order to assess the mathematical algorithms involved in TENA SmartCare Change Indicator.
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1 LIST OF ABBREVIATIONS

ADE – Adverse Device Effect
AE – Adverse Event
ASADE – Anticipated Serious Adverse Device Effect
CIP – Clinical Investigational Plan
FAS – Full Analysis Set
PPS – Per Protocol Set
SADE – Serious Adverse Device Effect
SAE – Serious Adverse Event
SAF – Safety Analysis Set
SAP – Statistical Analysis Plan
USADE – Unanticipated Serious Adverse Device Effect

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 B, date 19-Jul-2019 (Ref 1.) for the FUEL explorative clinical investigation. 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

The primary objective is to collect real-life measurement data using the Urine Sensor to assess the mathematical algorithms for wetness detection in TENA absorption products by urine volume quantification and [redacted] measurements.

3.1.2 Secondary objective

The secondary objective is to evaluate safety through analyzing device-related adverse events reported during the investigation.

3.2 Clinical Investigation Design

The clinical investigation will be carried out in the nursing home Tre Stiftelser in Gothenburg and include subjects affected with Urinary Incontinence (UI). In total 15 subjects are estimated to be enrolled in the exploratory clinical investigation. The clinical investigation is designed to be conducted in a controlled professional environment for a duration of 8 weeks. The clinical investigation involves two visits; one screening visit and one follow-up visit, as well as absorbent product related data capturing between these visits. The follow-up visit will be scheduled in conjunction with the completion of data capturing.

The purpose of this exploratory clinical investigation is to evaluate safety and to collect real-life measurement data using the TENA Urine Sensor (placed on allocated TENA incontinence products). The collected data will be used to assess the device related algorithms. The primary algorithms have been established and verified in a laboratory environment. However, several parameters differ between real-life and laboratory settings and can therefore be hard to predict. Consequently, real-life measurement data has been determined necessary to continue the product development.

To assess the mathematical algorithms, the urine volume in the incontinence product needs to be quantified (ml urine) and the [redacted] values from the Urine Sensor captured. Data such as; date and time of incontinence product application, date and time of removal, Urine Sensor ID, absorbent product information (type, absorption level and size), leakage outside product, presence of feces, and subject's main position since last absorbent product change will be recorded by the caregiver on a label located on a plastic bag. The absorbent product is thereafter placed in the plastic bag and provided to a Sponsor' representative. The plastic bag is weighted on a calibrated scale by the Sponsor' representative and the weight documented in the electronic Case Report Form (eCRF). The urine spreading in the absorbent product is documented by taking a photo of the absorbent area of the product.

3.3 Number of Subjects

The aim is to enroll 15 subjects (20% drop-out rate) to capture [redacted] measurement points during a period of 8 weeks ([redacted] measurement points per product type, and 9 product types in total).

3.4 Methods of Assigning Subject to Device Groups

FUEL explorative clinical investigation is a single-arm clinical investigation with no planned subgroup analyses.

Each participating subject will be provided with one or two TENA Urine Sensors (depending on incontinence product allocation), as well as absorbent products for the duration of the investigation. Nine types of absorbent products will be tested in the FUEL clinical investigation, and each participating subject will be allocated to the type(s) that are considered most suitable. What type(s) are most suitable will be decided during the screening visit depending on previous absorption product use and the subject's physiology.

3.5 Blinding

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

4 STATISTICAL AND ANALYTICAL PLANS

As FUEL is an explorative clinical investigation results will be summarized using relevant descriptive statistics such as mean, standard deviation (SD), median, minimum and maximum values and frequency tables. The data will later be used to assess the mathematical algorithms for the TENA SmartCare Change Indicator.

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

4.1 Sample Size Justification

No formal sample size calculation has been performed. Instead, it has been assumed that at least [redacted] measurement points (absorptions product registrations) will be required per product type to be in an accuracy range similar to the lab verified urine sensor accuracy (Ref 2.). Included in the assumptions for the [redacted] measurement points are also that each subject use 3 absorbent products each day and that 1/3 of the absorbent products will be disregarded due to faecal events or other failures.

In total 9 product types (3 products with 3 absorption levels each) will be evaluated resulting in a need of [redacted] measurement points. It is estimated that at least 12 subjects are considered appropriate to adapt for individual spreading during the test. However, to compensate for drop-outs or non-compliance 15 subjects were considered appropriate to include in the investigation.

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 consist of all consented subjects with at least one product registration.

4.2.3 Eligible Absorbent Product Information Registration Set

The Eligible Absorbent Product Information Registration Set will consist of registrations collected from the FAS that does not fulfill the following criteria:

- No predicted value was calculated by the algorithm
- Feces in the product
- Missing data for weight, sensor, gateway IDs
- Data excluded during the clean file meeting

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 the Eligible Absorbent Product Information Registrations Set.

4.3 Definition of Baseline

Baseline measurement is defined as the latest measurement prior to the first incontinence product registration. Baseline data will in general be presented using summary statistics as further explained below.

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. Table with summary statistics will be divided by product type and visit where applicable. Patient data listings will be sorted by product type, subject and timing of assessments.

4.5 Significance Level

Not applicable as no formal statistical analyses will be performed for this clinical investigation.

4.6 Multiple Comparisons/Multiplicity

Not applicable. No adjustment for multiplicity of testing will be done.

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 as no adjustment for covariates is planned.

4.9 Multicenter Studies

Not applicable. Only one site involved in the FUEL explorative clinical investigation.

4.10 Examination of Subgroups

Not applicable. 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
- Bedridden/not bedridden

Incontinence product(s) of use the previous 6 months, relevant concomitant medication, relevant medical and surgical history, evaluation of health status, urine pregnancy test and allocation to suitable absorbent products 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 Urine Sensor and TENA Gateway.

6.2 Placebo Treatment

Not applicable as no placebo treatment is involved.

6.3 Extent of Exposure

The exposure of study products for each subject was estimated to 6 weeks. Due to delayed data collection it was decided to prolong the study. As a consequence, the subjects will be exposed to the study products for approximately 10 weeks in total.

6.4 Compliance of Study Product

Compliance of study product will be presented by total number of occasions each subject has used the TENA Urine Sensor, e.g. number of incontinence registrations.

6.5 Concomitant Medications

Relevant concomitant medication data will be listed per subject.

7 STATISTICAL METHODOLOGY

Statistical analysis on variables of interest, including subject demographics, baseline characteristics, safety and performance endpoints will be summarized descriptively only. No comparisons will be made and hence no statistical tests performed.

7.1 Primary endpoint

Summarize the individual differences (predicted urine volume - true urine volume) using descriptive statistics. The predicted and true urine volumes will later be used to optimize mathematical algorithms for the TENA SmartCare Change Indicator.

7.1.1 Definition

The predicted urine volume is calculated from urine sensor values and the urine volume is determined from absorbent product weights.

7.1.2 Analysis

No statistical tests will be performed.

7.1.3 Presentation

Results will be presented using descriptive statistics.

7.2 Secondary Endpoint/safety endpoint

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

7.2.1 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 see the FUEL CIP version B 19-Jul-2019.

Adverse Event (AE)
Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

NOTE 1: This definition includes event 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 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.

Serious Adverse Event (SAE)
Adverse event that

a) led to a death,
b) led to 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) 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,

c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE: 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.

7.2.2 Analyses

The safety endpoint will be summarized using descriptive statistics.

7.2.3 Presentation

AE/ADE:

The following summaries of AEs and SAEs will be given by treatment and in total:

- 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 investigational product

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 investigational product, 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.

7.3 Interim Analysis

Not applicable. No interim analysis planned.

8 CHANGES FROM THE CIP

The study was prolonged due to delayed data collection. The subject's participation within the study was amended from 6 to approximately 10 weeks in total.

9 STATISTICAL DELIVERABLES

The following documents will be delivered:

- Statistical Analysis Plan (SAP)
- Descriptive statistics and summary tables
- Raw data in later specified formats.
- Listings for all data up to the final visit
  - Discontinued patients
  - CIP deviations
  - Patients excluded
  - Demographic
  - Exposure to study product
  - Adverse event

10 SOFTWARE

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

11 REFERENCES

Ref 1. (LUCY-051) FUEL Clinical Investigation Plan, version B, 19-Jul-2019

Ref 2. (ENG-333) Sensor verification and wetness detection report.

12 APPROVAL

Issued by:

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Date (dd-Mmm-yyyy)

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