Statistical Analysis Plan (SAP)

Protocol Title:	An Open-label, Prospective Trial Assessing Positive Detection Accuracy and Detection Latency Measures of the Miniature Ingestible Event Marker Tablet Using the D-Tect Patch in Healthy Subjects and Assessing Detection Latency Measures Using the D-Tect Patch in Subjects With Serious Mental Illness Taking Abilify MyCite Tablet
Protocol Version No./Date:	1.0/18-APR-2023
CRF Version No./Date:	1.3/02-JUN-2023
SAP Version No./Date:	1.0/22-JUN-2023

1.0 Approvals

Sponsor	
Sponsor Name:	Otsuka Pharmaceutical Development & Commercialization, Inc.
Representative/ Title:	PPD / Director, Global Clinical Development
Signature /Date:	
Representative/ Title:	PPD / Senior Director, Head of Biostatistics
Signature /Date:	
Representative/ Title:	PPD / Biostatistics Lead for Digital Medicine (Abilify MyCite)
Signature /Date:	
ICON	
Biostatistician / Title:	PPD / Senior Biostatistician
Signature /Date:	

(NOTE: Electronic Signatures should only be used if all parties have the ability to eSign.)

2.0 Change History

Version/Date	Change Log
1.0	Final Version 1.0

3.0 Table of Contents

4.0 Purpose

The Statistical Analysis Plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under Otsuka Pharmaceutical Development & Commercialization, Inc's Protocol 031-201-00521 dated 18-APR-2023.

5.0 Scope

The Statistical Analysis Plan outlines the following:

- Study Objectives
- Study Design
- Applicable Study Definitions
- Statistical Methods

6.0 Introduction

This SAP should be read in conjunction with the study protocol and case report form (CRF). Any further changes to the protocol or CRF may necessitate updates to the SAP.

6.1 Changes from Protocol

There are no major discrepancies between protocol and SAP, only the following minor differences are described:

1. Population definitions (SCR, FAS, FAS-Cohort 1, and FAS-Cohort 2) added, the protocol specified the intent-to-treat population, however, the full analysis set will be used.
2. The unanticipated adverse device effects stated in the protocol removed from the analysis.
3. AEs leading to discontinuation of the investigational device removed from analysis, instead AEs leading to study discontinuation will be analyzed.

7.0 Study Objectives

7.1 Primary Objective

The primary objectives of this study are:

- To evaluate positive detection accuracy (PDA) for the D-Tect Patch.
- To evaluate detection latency measures for the D-Tect Patch.

7.2 Secondary Objective

The secondary objective of this study is to collect and characterize AEs associated with the device.

8.0 Study Design

This two-cohort, open-label, prospective trial is designed to assess the PDA and detection latency of the D-Tect Patch. The PDA is defined as the proportion of miniature ingestible event marker tablets (MITs) detected out of the total ingestible event marker (IEM) detections of tested D-Tect Patches (Cohort 1 only). For detection latency, Patch Detection Latency, Ingestion Data Transfer

Latency, and Total Detection Latency will be measured for both cohorts (i.e., MITs and Abilify MyCite).

Cohort 1 will be completed in adult, healthy subjects. Subjects with difficulty swallowing, active skin infection or history of inflammatory skin condition, or an allergy to adhesive bandages/tapes will be excluded from participation. Subjects in Cohort 1 will take the MIT dose form. A minimum of 24 healthy subjects will be tested to obtain a minimum of 360 miniature ingestible event marker tablet ingestions for Cohort 1. This trial will consist of up to 3 onsite visits including:

- Visit 1: Screening
- Visit 2 (Day 1): Testing, patch placement, directly observed ingestion (DOI) of MITs (conducted either on the same day as Visit 1 or up to 7 days after Visit 1)
- Visit 3 (Day 8): In-person safety follow-up and removal of patch (conducted approximately 7 days [+ 2 days] after applying the D-Tect Patch).

Cohort 2 will be completed in adults with serious mental illness (SMI) who are prescribed and taking aripiprazole prior to trial entry. Subjects with difficulty swallowing, active skin infection or history of inflammatory skin condition, or an allergy to adhesive bandages/tapes will be excluded from participation. Subjects will take a single dose of Abilify MyCite at the same dose as the subject's current aripiprazole prescription. Subjects will be instructed not to take their currently prescribed dose of aripiprazole at home on Day 1 of the trial when Abilify MyCite will be ingested. A minimum of 30 subjects with SMI will be tested to obtain a minimum of 30 Abilify MyCite ingestions for Cohort 2. This trial will consist of up to 3 onsite visits including:

- Visit 1: Screening
- Visit 2 (Day 1): Testing, patch placement, DOI of a single dose of Abilify MyCite (conducted either on the same day as Visit 1 or up to 7 days after Visit 1)
- Visit 3 (Day 8): In-person safety follow-up and patch removal (approximately 7 days [+ 2 days] after applying the D-Tect Patch)

No trial procedures may be conducted prior to the signing of the informed consent form (ICF), which will occur at Visit 1. Visit 2 involves patch application and DOI(s). Visits 1 and 2 may be combined and conducted on the same day. Subjects will return to the site on Day 8 (+ 2 days), 7 days following patch placement for a safety follow-up evaluation and to make final observations of patch wear (Visit 3). Any patches that remain on the subject will be removed at this visit. Any patch that falls off prior to the safety follow-up visit should be retained by the subject and given to trial staff at the scheduled follow-up visit. A full Schedule of Assessments is included in **Table 1**.

Table 1: Schedule of Assessments (Cohorts 1 and 2)

Period	Screening	Testing	Follow-up
Visit	**Visit 1**	**Visit 2** [a]	**Visit 3** [b,c]
Trial Day	**Day −7 to Day 1**	**Day 1**	**Day 8 (+2 days)**
Informed Consent	X		

Demographics	X		
Medical History	X		
Concomitant Medications	X	X	X
Eligibility Criteria Review	X		
Vital Sign Measurements [d]	X		
Preparation of application site and patch placement		X	
Assessment of AEs [e]	X	X	X
Photograph of patches at application site [f]		X	X
DOI [g,h]		X	
Sleep Diary [i]		X	
Patch Removal [j]			X
Pregnancy Test [k]	X		

Abbreviations:
AE = adverse event; DOI = directly observed ingestion.

Footnotes:
[a] Conducted either on the same day as Visit 1, or up to 7 days after Visit 1.
[b] In-person safety follow-up to occur 7 days after applying the patch.
[c] If an in-person follow-up visit cannot occur due to COVID-19 restrictions, the site should conduct a follow-up visit via video conference to verbally assess subject safety and instruct the subject to remove the patch on Day 8.
[d] Vital sign measurements include blood pressure, heart rate, temperature, height, and weight.
[e] If an AE is related to the patch, then the Skin Irritation Scoring System (Table 8.6.1-1) will be completed by the investigator.
[f] A minimum of 3 patch placement photos are required: prior to initial dose, after completion of DOI(s), and when the subject returns for follow-up (prior to patch removal).
[g] Cohort 1: Subjects will ingest 15 miniature ingestible event marker tablets (MITs) over the course of 1 visit day (with approximately 15 [−5 / +15] minutes between ingestions).
[h] Cohort 2: Subjects will ingest a single dose of Abilify MyCite at the same dose as their currently prescribed aripiprazole.
[i] On Day 1 of the trial, subjects will be sent home with a sleep diary to complete each day until they return for the follow-up visit on Day 8 [+ 2 days].
[j] Any patch that falls off during the trial should be retained by the subject and given to trial staff during the in-person follow-up visit. All patches must be removed on Day 8, even if the clinic visit is delayed.
[k] To be collected from woman of childbearing potential via urine dipstick.

8.1 Sample Size Considerations

The study is exploratory in nature, the sample size is not determined based on a specific hypothesis or effect size.

For Cohort 1, a minimum of 24 subjects are planned to complete 15 DOIs per subject. With this assumption, 24 subjects with 360 ingestions will provide sufficient power to ensure the lower bound of the 95% confidence interval (CI) for PDA is at 95% assuming the PDA rate of 97.3% of the D-Tect Patch using binomial distribution.

For Cohort 2, there is no formal sample size calculation. A minimum of 30 subjects are planned to complete a single DOI of Abilify MyCite.

8.2 Randomization

Randomization is not applicable to this study.

9.0 Study Estimands

The 'Estimands' framework is used to define the treatment effect of interest in a clinical trial, which specifies how the treatment effect is to be estimated, and what assumptions are necessary to make the estimation valid. In this study, the treatment effect, as well as the potential sources of bias or variability that may impact the estimation of treatment effects, are not the research question of interest. The objective of this study is to assess the PDA and detection latency of the D-Tect Patch in an exploratory manner, therefore, the estimands in this study are not applicable.

9.1 Endpoints

Objectives	Endpoints
Primary	Primary endpoint for PDA
• Evaluate PDA and detection latency measures for the D-Tect Patch.	• Estimate PDA with the CI lower limit greater than 95% when a subject is wearing the D-Tect Patch.
	Primary endpoint for Detection Latency
	• The mean and median for three latency measures: Patch Detection Latency, Ingestion Data Transfer Latency, and Total Detection Latency (See **Section 10.7** for detailed definition).
Secondary	Safety
• To collect and characterize AEs associated with the device.	• The frequency and severity of AEs, device-related AEs, serious AEs (SAEs), and AEs leading to discontinuation

9.2 Population Sets

9.2.1 Screened Analysis Set

The **Screened Analysis Set (SCR)** will consist of all subjects who sign an ICF. This analysis set will be used to report disposition and screening failures.

9.2.2 Enrolled Analysis Set

The **Enrolled Analysis Set (EAS)** will consist of all subjects who sign an ICF and enter the trial (and only subjects who meet all the inclusion criteria and none of the exclusion criteria).

9.2.3 Full Analysis Set

The **Full Analysis Set (FAS)** comprises all the detections of the wearable sensors done on the subjects who took at least 1 dose of MITs (Cohort 1) or Abilify MyCite (Cohort 2), excluding those detections with device malfunction (invalid session and impedance is bad).

For the primary endpoint in Cohort 1, the **FAS-Cohort 1** is a subset of the FAS and consists all the detections for subjects who took at least 1 dose of MITs (Cohort 1).

For the primary endpoint in Cohort 2, the **FAS-Cohort 2** is a subset of the FAS and consists all the detections for subjects who took at least 1 dose of Abilify MyCite (Cohort 2).

9.2.4 Safety Analysis Set

The **Safety Analysis Set (SAF)** will consist of all subjects who wear any patch or take any tablet from the trial and have any safety assessment.

9.2.5 Summary of Analysis Sets

Analyses	SCR	EAS	FAS-Cohort 1	FAS-Cohort 2	SAF
Subject disposition		✓			
Demographic and baseline characteristics		✓			
Medical history		✓			
Prior and concomitant medications		✓			
Directly Observed Ingestion			✓	✓	
Study Drug Exposure				✓	
Patch Application and Removal			✓	✓	
Protocol deviation		✓			
Positive Detection Accuracy			✓		
Detection Latency Measures			✓	✓	
Adverse Events	✓				
Treatment-Emergent Adverse Events (TEAEs)					✓
Deaths and Serious TEAEs					✓
Vital Signs					✓

Abbreviations:

SCR = Screened Analysis Set,

EAS = Enrolled Analysis Set,

FAS = Full Analysis Set,

SAF = Safety Analysis Set

10.0 Conventions and Derivations

10.1 Visit Windows

Table 2 shows study periods, visits, study days, and visit windows. The visit will be used for analysis according to the visit reported by the CRF.

Table 2: Study Visit Window

Study Period	Study Visit	Study Day	Study Visit Window
Eligibility screening	Visit 1	-7 to 1	-
Testing	Visit 2	1	-
Follow-up	Visit 3	8	+ 2 days

Study day will be calculated as

Study Day = Date of day – Date of Testing + 1

10.2 Unscheduled Visit Definition

An **Unscheduled Visit** is defined as any additional visit performed at the investigator's discretion, at any time between Testing (Day 1) and the Follow-Up Visit at Day 8.

10.3 Prior and Concomitant Medication

In this study, all medications and therapies taken by the subject from 7 days prior to D-Tect Patch application through the end of the evaluation period (defined as the time period during which subjects are evaluated for primary and/or secondary objectives) will be recorded.

A medication is considered to be prior if the start date and time is before the first ingestion date and time. A medication is considered to be concomitant if the medication is ongoing at, started together with, or started after the first ingestion date and time. Note that a medication can be considered both prior and concomitant.

10.4 Definition of Body Mass Index

The BMI (Body Mass Index) calculation divides a subject's weight in kilograms by their height in meters squared. The formula to calculate BMI is as follows:

BMI = weight (in kilograms) / (height (in meters))^2

International System of Units for weight in kilogram (kg) and height in meter (m) will be used in analysis, the formulas for converting units of weight and height are as follows:

Weight in kilograms (kg) = Weight in pounds (lb) × 0.45359237

Height in meters (m) = Height in inches (in) × 0.0254

10.5 Definition of Treatment-Emergent Adverse Event

TEAEs are defined as AEs that occurred on or after the subject wears any patch or takes any tablet from the trial at test day, and the AEs that occurred before the subject wears any patch or takes any tablet and are worsening, serious, related, or resulted in death, discontinuation, or interruption of investigational product. All other AEs recorded in CRF are considered Non-Treatment-Emergent Adverse Events (Non-TEAEs).

10.6 Definition of Positive Detection Accuracy

The Positive Detection Accuracy (PDA) is defined as $\boldsymbol{PDA = k/n}$, where $\boldsymbol{n}$ is the number of the total DOIs in FAS-Cohort 1 (malfunction sessions have been excluded from FAS-Cohort 1), and $\boldsymbol{k}$ is the number of total positive detections by the patch.

10.7 Definition of Detection Latency

As shown in the system diagram in **Figure 1**, there are 4 time-stamped events (TSEs) associated with measuring detection latency shown in **Table 3**.

Table 3: Time-stamped events (TSEs) associated with measuring detection latency

TSE 1	Subject takes tablet. Directly observed ingestion time is recorded by the clinician.
TSE 2	Tablet sends signal to the patch. Tablet is detected & recorded by the patch as an IEM record with a timestamp.
TSE 3	Patch sends ingestion data to phone. The tablet ingestion data is communicated to and recorded by the mobile device as a pill-ingestion-metric with a timestamp.
TSE 4	Tablet ingestion data is displayed. The tablet display event is triggered on the mobile device as a pill-display-event with a timestamp.

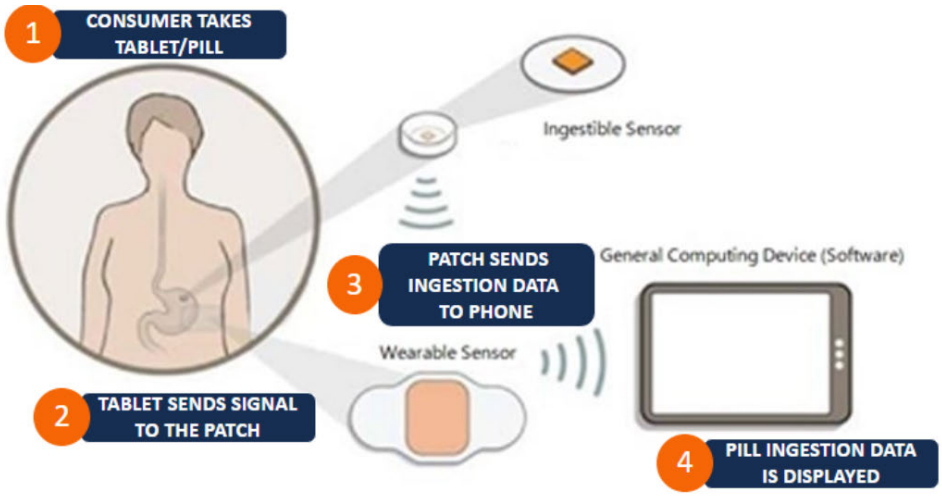

Figure 1: Digital Medicine System

The latency measurements between each of above timestamps are defined in **Table 4**.

Table 4: Latency measurements

Latency Measurements	Definition	Maximum Observation Time
Patch Detection Latency	Time between TSE 1 and TSE 2 in seconds	10 minutes/600 seconds
Ingestion Data Transfer Latency	Time between TSE 2 and TSE 4 in seconds	5 minutes/300 seconds
Total Detection Latency	Time between TSE 1 and TSE 4 in seconds	15 minutes/900 seconds

For Kaplan-Meier estimate, if the DOI is successfully detected, it will be treated as positive detection and event = "1"; If the DOI is not successfully detected or latencies have been larger than the maximum observation time (defined above in **Table 4**), the data will be considered as censored data and event = "0", where time to event is defined as maximum observation time.

10.8 Missing Data

All statistical analysis will be based on observed values. Missing values will not be imputed.

11.0 Interim Analyses

No interim analysis is planned in this study.

12.0 Statistical Methods

All analyses will use SAS® version 9.4 or higher. Table and listing outputs will be presented using ICON standard layouts.

Unless specified otherwise, categorical variables will be summarized using counts and percentages (n [%]). Percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places and percentages will not be displayed for zero counts.

Continuous variables will be summarized using the number of observations (n), mean, and standard deviation, median, minimum, and maximum. The minimum, and maximum values will be displayed to the same level of precision as the raw data; the mean and the median to a further decimal place; and the standard deviation to two additional decimal places to a maximum of four.

In listings, data will be presented with the same precision as the original data.

Unless specified otherwise, all the tables will be produced by cohort, and overall will not be displayed.

Unscheduled visits will not be summarized or included in any analysis but will be included in listings outputs.

12.1 Subject Disposition

The following information will be summarized for subject disposition by cohort in table based on **SCR** Analysis Set:

- Number and percentage of subjects screened,

- Number and percentage of screening failures and corresponding reasons for screening failure,
- Number and percentage of subjects included in each analysis set (EAS, FAS, and SAF).

Furthermore, following information will be provided by cohort in tables based on **EAS**.

- Number and percentage of subjects who complete all the ingestions,
- Number and percentage of subjects who complete study,
- Number and percentage of discontinuations from study and corresponding reasons for discontinuation,

The following reasons - as specified in the CRF - will be included in the disposition tables and in a listing (Listing: Enrollment and Study Completion for **SCR** Analysis Set):

Reasons for Screening Failure:

1. Failed Inclusion Criteria
2. Met Exclusion Criteria
3. Death
4. Adverse Event
5. Physician Decision
6. Pregnancy
7. Protocol Deviation
8. Terminated by Sponsor
9. Withdrawal by Subject
10. Other

Reasons for Study Discontinuation:

1. Death
2. Adverse Event
3. Lost to Follow-up
4. Non-compliance with Device/Patch
5. Physician decision
6. Pregnancy
7. Protocol Deviation
8. Terminated by Sponsor
9. Withdrawal by Subject
10. Withdrawal of Consent

11. Other

12.2 Demographic and Baseline Characteristics

The following demographic and baseline data will be summarized in a table by cohort for the **EAS**.

- **Age** at informed consent (in years).
- **Sex at Birth**: Female; Male.
- **Gender Identification**: Female; Male; Transgender Man; Transgender woman; Gender non-conforming; None of the above; Prefer not to answer; Other.
- **Race**: American Indian or Alaska Native; Asian; Black or African American; Native Hawaiian or Other Pacific Islander; White; Other.
- **Ethnicity**: Hispanic or Latino; Not Hispanic or Latino; Other; Unknown.
- **Childbearing Potential**: Yes; No (the percentage of childbearing potential is based on the number of Females at birth).
- **Weight** (kg)
- **Height** (m)
- **BMI** (kg/m²)

The demography and baseline data captured in the CRF will be included in a listing for **EAS** only.

12.2.1 Medical History

General medical history will be presented in the table by cohort for **EAS**, and the psychiatric medical history will be analyzed in the same manner. The number and percentage of subjects with each medical history term will be summarized by the Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT). Medical history will be coded using MedDRA version 26.0 to assign a SOC and PT to each event.

Separate listings for general medical history and psychiatric medical history will be included for **EAS**.

12.2.2 Prior and Concomitant Medications

Medications received prior or concomitantly with study drug (preferred base name), categorized by Anatomical Therapeutic Chemical (ATC) medication subgroup (ATC level 4) or subgroup (ATC level 3, 2 or 1, if level 4 is not available) according to WHODRUG (Version Global B3 MARCH 2023), will be summarized separately in tables for **EAS**. The number and percentage of subjects using each medication will be displayed together with the number and percentage of subjects using at least one medication within each medication group and subgroup.

Prior and concomitant medications will be included together but with "Concomitant Flag" in a listing for **EAS**.

12.3 Device Application

12.3.1 Directly Observed Ingestion

The following directly observed ingestion (DOI) data for Cohort 1 will be summarized in Table together with positive detection (Section 12.5.1) and latency data (Section 12.5.2) for the **FAS-Cohort 1**.

- Number of ingestions (15 times; 14 times; 13 times; 12 times; 11 times; 10 times; 9 times; 8 times; 7 times; 6 times; 5 times; 4 times; 3 times; 2 times; Once)

Furthermore, the above information will be provided in a listing based on **FAS-Cohort 1** together with

- The reason if subject does not ingest the miniature IEM tablets
- Date of ingestion
- Time of each ingestion,
- Volume of water (mL) ingested with placebo,
- Detection data
    - Patch serial number
    - Detected (True/False)
    - Patch impedance good (True/False)
    - Valid session (True/False)
    - Invalid session description
    - False positive (True/False)
- Latency data
    - Patch serial number
    - Date and time of detected
    - Date and time displayed
    - Patch detection latency (seconds)
    - Ingestion data transfer latency (seconds)
    - Total detection latency (seconds)
- Did the subject complete all the ingestions
- Was the subject discontinued from completing all ingestions and the reason for discontinuation

12.3.2 Drug Exposure

Drug Exposure is not applicable for Cohort 1 because of placebo tablets.

For Cohort 2, subjects will ingest Abilify MyCite at the same dose as their currently prescribed aripiprazole. The following drug exposure data for Cohort 2 will be summarized in a table together with latency data for the **FAS-Cohort 2.**

- The number and percentage of Abilify Dose ingested (2 mg; 5 mg; 10 mg; 15 mg; 20 mg and 30 mg).

Furthermore, above information will be provided in a listing based on **FAS-Cohort 2**, together with

- Date of Abilify MyCite ingestion
- Time of Abilify MyCite ingestion
- Latency data
    - Patch serial number
    - Date and time of detected
    - Date and time displayed
    - Patch detection latency in seconds
    - Ingestion data transfer latency in seconds
    - Total detection latency in seconds
- The reason if subject does not ingest the current prescribed dose of Abilify MyCite
- Volume of water (mL) ingested with Abilify MyCite

12.3.3 Patch Application and Removal

As defined in **Table 1**, a minimum of three patch placement photos are required and recorded in the CRF: prior to initial dose, after completion of DOI(s), and when the subject returns for follow-up (prior to patch removal). The following data will be provided in listings for **FAS**:

- Photographs taken prior to initial dose (Yes or No; the reason if no; date and time of photography)
- Patch Application completed (Yes or No; the reason if no; date and time of completion)
- Photographs taken after DOIs (Yes or No; the reason if no; date and time of photography)
- Was the subject instructed to keep the patch on as long as possible? (Yes or No)
- Was subject instructed to return patch to the trial site during follow-up visit? (Yes or No)
- Photographs taken prior to patch removal (Yes or No; the reason if no; date and time of photography)
- Patch Removal completed (Yes or No; the reason if no; date of completion; Patch removal/fell off date and approximate time if it is not on the same date as the visit)
- Patch returned (Yes or No; the reason if no)

12.4 Protocol Deviations

The protocol deviations will be captured in CRF. Per protocol set is not applicable in this study, and no data review meeting is planned prior to database lock to finalize the evaluable subjects set. All protocol deviations will be listed only based on **EAS**.

12.5 Primary Analyses

The primary analyses including Positive Detection Accuracy and Detection Latency Measures are described in the following sections.

12.5.1 Positive Detection Accuracy

For **FAS-Cohort 1**, the number of positive detections, the positive detection accuracy (PDA) and 95% Clopper-Pearson confidence interval (CI) will be summarized, for overall DOIs only.

Positive detections will not be reported in CRF and will rather be downloaded from the trial mobile device(s). All positive detections data will be listed together with directly observed ingestion data (**Section 12.3.1**) based on **FAS-Cohort 1**.

12.5.2 Detection Latency Measures

As defined in **Table 3**, the directly observed ingestion time (TSE 1) is recorded in the CRF. Other signal detection times (TSE 2-4) will be downloaded from the trial mobile device(s) for analysis. The derivation of detection latency measures, including Patch Detection Latency, Ingestion Data Transfer Latency, and Total Detection Latency, are provided in **Table 4**.

The three detection latency measures for all DOIs will be summarized using descriptive statistics, for **FAS-Cohort 1** and **FAS-Cohort 2** separately.

Furthermore, two Kaplan-Meier curves will be plotted for all of the latency times (all DOIs), for **FAS-Cohort 1** and **FAS-Cohort 2** separately. The three detection latency measures will be displayed as three curves on the plot. A table will be provided to show the summary of survival status, the median (50% survival time), and 25% and 75% percentiles of survival by Kaplan-Meier estimate.

12.6 Safety Analyses

All safety analyses will be presented for the **SAF**.

12.6.1 Treatment-Emergent Adverse Events

All AEs reported in the CRF will be coded using MedDRA.

An overall summary of TEAEs, including the number of events reported, and the number and percentage of subjects will be prepared by cohort in a table, as specified below:

- Subjects reporting at least 1 TEAE
- Subjects reporting at least 1 serious TEAE
- Subjects reporting at least 1 device/patch related TEAE
- Subjects reporting at least 1 device/patch related TEAE (by skin irritation score from 0-7)

- Subjects reporting at least 1 clinically significant TEAE (defined by skin irritation score ≥ 2)
- Subjects reporting at least 1 Abilify MyCite treatment related TEAE (Cohort 2 only)
- Subject reported receiving at least 1 TEAE with concomitant or additional therapy
- Subjects with any TEAE leading to death
- Subjects discontinuing the study due to a TEAE
- Subjects discontinuing the study due to a device/patch related TEAE
- Subjects discontinuing the study due to an Abilify MyCite treatment related TEAE

Furthermore, a breakdown of the number and percentage of subjects reporting TEAE, categorized by system organ class (SOC) and preferred term (PT) coded according to the MedDRA dictionary (Version 26.0), will be presented. Note that counting will be by subject not event and subjects are only counted once within each SOC or PT. Therefore, when counting the number of subjects with each event, subjects with multiple events within a particular SOC or PT will be counted under the category of their most severe event within that SOC or PT. The list of TEAE tables is the following:

- TEAEs by SOC and PT
- Clinically significant TEAEs (defined as device/patch related TEAE and skin irritation score ≥ 2) by SOC and PT
- Any TEAE by maximum severity (mild, moderate, severe) by SOC and PT
- Any TEAE related to study device/patch by SOC and PT
- Any TEAE related to Abilify MyCite treatment by SOC and PT (Cohort 2 only)
- Serious TEAEs by SOC and PT
- TEAE leading to death by SOC and PT
- TEAEs leading to study discontinuation by SOC and PT

All AEs recorded on the CRF will be listed with MedDRA SOC and PT. The TEAEs will be marked with a flag within the listing. A footnote will state if no AE occurred after screening and before the subject wore any patches or took any tablet.

Independent listings will be provided with MedDRA SOC and PT for:

- Device/Patch related TEAEs (with skin irritation score evaluation),
- Abilify MyCite treatment related TEAEs (Cohort 2 only),
- TEAEs leading to study discontinuation

12.6.2 Deaths and Serious TEAEs

As already described in previous section, a summary table for TEAE leading to death and for serious TEAEs will be provided by SOC and PT.

A listing for all serious TEAEs and for all TEAE leading to death will be prepared.

12.6.3 Laboratory Data

Laboratory data is not applicable in this study.

12.6.4 Vital Signs

Vital sign measurements will be collected at Screening (Visit 1) only, the following vital signs will be summarized in a table:

- Systolic Blood Pressure (mmHg)
- Diastolic Blood Pressure (mmHg)
- Heart Rate (bpm)
- Body Temperature (Fahrenheit)

Vital signs data including abnormal and clinically significant results will be provided in a listing.

13.0 Glossary of Abbreviations

Glossary of Abbreviations:	
AE	Adverse event
ATC	Anatomic Therapeutic Chemical
CI	Confidence Interval
COVID-19	Coronavirus disease 2019
CRF	Case Report Form
DOI	Directly Observed Ingestion
EAS	Enrolled Analysis Set
FAS	Full Analysis Set
ICF	Informed Consent Form
IEM	Ingestible Event Marker
MedDRA	Medical Dictionary for Regulatory Activities
MIT	Miniature ingestible event marker tablet
PDA	Positive Detection Accuracy
SAP	Statistical Analysis Plan
SAE	Serious Adverse Event
SAF	Safety Analysis Set
SCR	Screened Analysis Set
SMI	Serious Mental Illness

SOC	System Organ Class
PDA	Positive Detection Accuracy
PT	Preferred Term
TEAE	Treatment-Emergent Adverse Event
TSE	Time-Stamped Event

This page is a manifestation of an electronically captured signature

SIGNATURE PAGE

Document Name: OTABEV04-0D1P6W_Statistical Analysis Plan (SAP) text v1.0

Document Number: CCI [redacted]

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:min) - UTC timezone
PPD	Clinical Approval	28-Jun-2023 16:30:12
	Biostatistics Approval	28-Jun-2023 13:25:56