Statistical Analysis Plan: 60128116

Study Title:	TIMMY3 80601-2-56:2017 + A1 2018
Study Number:	60128116
Study Design	This is a multi-clinician, multi-center, multi-person, non-randomized study to validate the clinical accuracy of the TIMMY3 thermometer algorithm on all age groups in the oral, adult axillary, pediatric axillary, and rectal temperature modes in 420 patients per ISO 80601-2-56:2017 + A1:2018.
Product Name:	TIMMY3 Investigational Device (Integrated into host device Connex Vital Signs Monitor)
Indication:	TIMMY3 provides interfaces to allow the host device to implement predictive and direct measurements of the oral, axillary, and rectal subject sites.
Statistician:	[redacted]
Sponsor:	[redacted]
Responsible Medical Officer:	[redacted]
Final Date:	25 MAR 2025

Confidentiality Statement

[redacted]

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SIGNATURE PAGE

Study Title: TIMMY3 80601-2-56:2017 + A1 2018

Study Number: 60128116

Statistician: [redacted]

I have read this report and confirm that to the best of my knowledge it accurately describes the planned analyses of the study.

Signature: [redacted]

Email: [redacted]

Prepared by: [redacted] Date: [redacted]

Signature: [redacted]

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Approved by: [redacted] Date: [redacted]

Signature: [redacted]

Email: [redacted]

Approved by: [redacted] Date: [redacted]

Signature: [redacted]

Email: [redacted]

Approved by: [redacted] Date: [redacted]

REVISION HISTORY

Version	Revision Summary	Reason(s) for Revision
1.0	Initial release	N/A
2.0	Amendment 1	Updated analysis populations. Added ISO analysis sets and removed Per Protocol Set (PPS). Updated patient disposition based on revised analysis populations. Updated primary endpoint analysis section to include potential sensitivity analysis to be performed if any non-compliance is identified. Removed sensitivity analysis on PPS. Updated TLF numbering and analysis populations.
3.0	Amendment 2	Updated analysis populations. Removed Full Analysis Set (FAS) and updated ISO analysis sets. Updated Appendix 1: List of Tables, Listings, and Figures to remove FAS Corrected typo in 2.4.1.2 Analysis of Primary Efficacy Endpoint Updated references of Device Deficiencies to Unanticipated Problems to stay aligned with CRF

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
AS	Adult Axillary ISO Analysis Set
CVSM	Connex Vital Signs Monitor
DD	Device Deficiency
DUT	Clinical Thermometer under Test
eCRF	Electronic Case Report Form
ID	Identification
IFU	Instructions for Use
ISO	International Organization for Standardization
OS	Oral ISO Analysis Set
PS	Pediatric Axillary ISO Analysis Set
PT	Preferred Term
RCT	Reference Clinical Thermometer
RS	Rectal ISO Analysis Set
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SS	Safety Analysis Set
UADE	Unanticipated Adverse Device Effect

1. STUDY DETAILS

This statistical analysis plan (SAP) is provided to describe the framework for the reporting, summarization, and statistical analysis methodology of the safety and efficacy parameters measured throughout the study. It is based on clinical trial protocol 60128116, Version C, dated 21 OCT 2024.

1.1 Study Objectives and Endpoints

1.1.1 Study Objective

The primary objective is to validate the clinical accuracy of the TIMMY3 thermometer algorithm on all age groups in the oral, adult axillary, pediatric axillary, and rectal temperature modes. Clinical accuracy will include measurement of clinical bias, with its limits of agreement, and clinical repeatability as defined by the International Organization for Standardization (ISO) 80601-2-56:2017 + A1:2018.

1.1.2 Primary Endpoint

The primary endpoint is clinical accuracy as defined by the ISO 80601-2-56:2017 + A1 2018. Clinical accuracy is the closeness of agreement between the output temperature of a clinical thermometer and the true value of the temperature of the reference body site that the clinical thermometer purports to represent. Clinical accuracy will include measurement of clinical bias, with its limits of agreement, and clinical repeatability[1].

1.2 Study Design

1.2.1 Overall Study Design and Plan

This is a multi-clinician, multi-center, multi-person, non-randomized study to validate the clinical accuracy of the TIMMY3 thermometer integrated into the CVSM algorithm on all age groups in the oral, adult axillary, pediatric axillary, and rectal temperature modes. Clinical accuracy validation is conducted in accordance with ISO 80601-2-56:2017 + A1:2018.

Approximately 420 patients will be enrolled in the US.

The study design includes the following:

- All temperatures will be measured in °C.
- Subjects will be screened for study eligibility by determining that no contraindications to temperature measurement (as appropriate per oral, rectal, or axillary site) exist.
- Study subjects may only be enrolled once per anatomical site. A single subject may be enrolled in the oral, and/or axillary, and/or rectal site.
- For oral, rectal, or axillary sites, each enrolled subject will undergo a predictive (adjusted) mode temperature measurement followed immediately by a Monitor (Direct) mode temperature measurement with the same instrument, without moving the probe position. Monitor (Direct) mode temperature must be 3 minutes for oral and rectal temperatures and 5 minutes for axillary temperatures. The Monitor (Direct) mode temperature will be timed by a calibrated stopwatch. The following 2 predictive

(adjusted) temperatures will be acquired in the same site with a minimum of 1 minute in between readings using a calibrated stopwatch.

- The clinicians will wait a minimum of 3 minutes before taking the next temperature on a different subject with the same probe. This will minimize the possibility of collecting data from a site or a probe still physiologically impacted by the previous temperature measurements.
- [redacted] Subsequent reports will in no way identify a subject.
- The total duration of subject participation in this study may last approximately 20-30 minutes for the collection of a data set per anatomical site.

The Connex Vital Signs Monitor (CVSM) thermometer operates in a Predictive (Adjusted) Mode and a Monitor (Direct) Mode. Predictive (Adjusted) mode temperatures are determined by measuring the rate of change of the sensor's output and using that information to anticipate or predict the final equilibrium temperature for the site it is measuring.

- Oral Reference Temperature is defined as 3-minute monitor (Direct) mode temperature taken in the left or right posterior, medial, sublingual pocket. The oral reference temperature will be done on subjects 5 years of age and older.
- Rectal Reference Temperature is defined as 3-minute monitor (Direct) mode temperature taken in the rectum. The rectal reference temperature will be done on subjects of all ages.
- Adult Axillary Reference Temperature is defined as 5-minute monitor (Direct) mode temperature taken in left or right axilla. The adult axillary reference temperature will be done on subjects 18 years of age and older.
- Pediatric Axillary Reference Temperature is defined as 5-minute monitor (Direct) mode temperature taken in left or right axilla. The pediatric axillary reference temperature will be done on subjects 17 years of age and younger.
- Note 1: Whenever possible temperatures will be obtained from subjects of all ages. Oral temperatures, however, may be inappropriate for children under 5 years of age since they may not be capable of keeping the probe in the mouth for three minutes.
- Note 2: Monitor (Direct) mode reading times will be timed using a calibrated stopwatch.
- Note 3: It is [redacted], based on 15 years of historical testing, that oral and rectal thermal equilibrium are attained in 3 minutes and axillary thermal equilibrium is obtained in 5 minutes.

1.2.2 Determination of Sample Size

A sample size of 420 for all 4 measurement modes (oral, pediatric axillary, adult axillary, or rectal) was determined per ISO 80601-2-56:2017 + A1:2018 - Human Subject population requirements. The total number of subjects per measurement mode is required to be at least 105[1]. This is a descriptive study, and no formal hypothesis testing is planned.

Table 201.102 — Subject age groups[1]

Age group	Age[11]
A1	0 up to 3 months
A2	3 months up to 1 year
B	older than 1 year and younger than 5 years
C	older than 5 years

At least 35 subjects are required for each age group A, B, and C if the measurement mode supports that age group. For group A there is an added requirement that subgroups A1 and A2 each need to have at least 15 subjects.

For any group or subgroup, a minimum of 30% and a maximum of 50% of the subjects need to be febrile.

Febrile is defined as follows:

- Oral febrile is defined as a 3-minute monitor (Direct) mode temperature of 37.5°C (99.5°F) or greater.
- Adult/Pediatric Axillary Febrile is defined as a 5-minute monitor (Direct) mode temperature of 37.2°C (99.0°F) or greater.
- Rectal febrile is defined as a 3-minute monitor (Direct) mode temperature of 38.0°C (100.4°F) or greater.

Oral supports age group C as 5 years old and greater. Pediatric axillary supports A1, A2, B, and C where C contains subjects between 5 years and less than 18 years old. Adult Axillary supports group C where C contains subjects 18 years old and greater. Rectal supports A1, A2, B, and C with no restrictions.

A single data measurement set is defined as 3 predictive (adjusted) mode test temperatures and a 3-minute (oral or rectal) or a 5-minute (adult/pediatric axillary) monitor (Direct) mode reference temperature.

For febrile subjects less than 5 years of age only one predictive (adjusted) mode measurement may be taken if the child is unable to tolerate an additional 2 predictive (adjusted) mode measurements. This will be at the discretion of the clinician doing the

temperatures if the child is not able to tolerate the 2 additional predictive temperature measurements.

1.2.3 Randomization Procedure

No randomization will occur for this study.

1.2.4 Blinding

This is an open-label study and will not have blinding of any investigational products.

1.3 Analysis Populations

Five main analysis sets are defined for this study.

1.3.1 Definition of Analysis Populations

ISO Analysis Sets:

Oral ISO analysis set (OS): The first 105 enrolled subjects (defined by chronological order of informed consent date and ascending order of subject ID) with an ISO and IFU compliant data set collected for the oral body site who collectively meet the ISO age group and febrile requirements and do not have any protocol deviations that could impact the primary endpoint.

Rectal ISO analysis set (RS): The first 105 enrolled subjects (defined by chronological order of informed consent date and ascending order of subject ID) with an ISO and IFU compliant data set collected for the rectal body site who collectively meet the ISO age group and febrile requirements and do not have any protocol deviations that could impact the primary endpoint.

Pediatric Axillary ISO analysis set (PS): The first 105 enrolled subjects (defined by chronological order of informed consent date and ascending order of subject ID) with an ISO and IFU compliant data set collected for the pediatric axillary body site who collectively meet the ISO age group and febrile requirements and do not have any protocol deviations that could impact the primary endpoint.

Adult Axillary ISO analysis set (AS): The first 105 enrolled subjects (defined by chronological order of informed consent date and ascending order of subject ID) with an ISO and IFU compliant data set collected for the adult axillary body site who collectively meet the ISO age group and febrile requirements and do not have any protocol deviations that could impact the primary endpoint.

An ISO compliant data set includes 3 consecutive measurement procedures, as indicated in the IFU, with the DUT and one temperature with an RCT for each subject. For febrile subjects less than 5 years of age, only one DUT measurement need be taken.

All febrile subjects with ISO and IFU compliant data sets will be included in the appropriate ISO analysis set, unless this exceeds the maximum febrile proportion allowed by the ISO guidelines. The remaining non-febrile subjects to be included in the ISO analysis set will be selected by chronological order of informed consent date and ascending order of subject ID.

Safety analysis set (SS): all patients who underwent measurement using the TIMMY3 thermometry module, regardless of whether a temperature measurement was obtained.

1.3.2 Protocol Deviations

Protocol deviations will be summarized for all enrolled patients pooled together. Patient counts will be presented for minor protocol deviations, major protocol deviations, and for each category of major protocol deviation.

Protocol deviations will also be listed for enrolled subjects. The listing will include patient id, age, verbatim description of the protocol deviation, the assigned category of protocol deviation, and major/minor status.

1.4 Interim Analysis

An interim analysis has not been planned for this study.

2. ANALYSIS METHODS

2.1 General Principles

Unless otherwise specified, summary statistics (n, mean, standard deviation [SD], median, minimum, and maximum values) will be presented for continuous variables. Counts and, if relevant, percentages will be presented for categorical variables.

Unless otherwise noted, all analyses will be performed using SAS/Graph® 9.4 software, SAS/STAT® 15.1 software, and BaseSAS® 9.4. Copyright © 2016, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. All Rights Reserved

Unless otherwise specified, the estimated mean and median for a set of values will be displayed to 1 more significant digit than the original values, standard deviations will be displayed to 2 more significant digits, and minimum and maximum values will be displayed with the same number of significant digits as the original values. If an original

value has more than 2 decimal places, the significant digits will be counted as if there are 2 decimal places. All percentages will be displayed with 1 decimal place unless more decimal places are needed to show 1 significant digit (i.e. a percentage of 0.01 will be shown as 0.01 as opposed to 0.0).

2.1.1 Completion and Discontinuation

A patient is considered to have completed the study when he/she ceases active participation in the study because the patient has, or is presumed to have, completed all study procedures according to the protocol. Any other cases are classified as discontinuation.

Reasons for completion/discontinuation will be reported on the Completion/Discontinuation electronic case report form (eCRF), including:

- Adverse Event
- Lost to Follow-up
- Voluntary withdrawal
- Investigator's Discretion
- Death
- Other

Regardless of the reason, all data available for the patient up to the time of completion/discontinuation should be recorded on the appropriate eCRF. The reason for discontinuation will be recorded and the data collected up to the time of discontinuation will be used in the analysis and included in the clinical study report.

2.2 Patient Disposition

Patient disposition will be summarized and will include:

- Number of patients who signed informed consent (enrolled)
- Number of patients who screen fail. These patients will also be summarized by primary reason for screen failure from the study. The percentage associated with each reason will have the total number of patients who screen fail as the denominator.
- Number of patients eligible for study measurements to be taken. This will be calculated by taking the number enrolled minus the number of screen failures.

- Number of patients who underwent measurement using TIMMY3 thermometry module, regardless of whether a temperature measurement was obtained (SS).
- Number of patients in at least one ISO analysis set
- Number of patients in the Oral ISO Analysis Set (OS).
- Number of patients in the Rectal ISO Analysis Set (RS).
- Number of patients in the Pediatric Axillary ISO Analysis Set (PS).
- Number of patients in the Adult Axillary ISO Analysis Set (AS).
- Number of patients who completed the study.
- Number of patients who discontinued (withdrew early) from the study. These patients will also be summarized by primary reason for withdrawal from the study. The percentages associated with each reason for early withdrawal will have the total number of patients who withdrew early as the denominator.

A listing of all patients enrolled in the study will be created including patient id, age, sex, whether the patient is in each of the analyses sets, completion status, reason for discontinuation (if applicable).

2.3 Demographics and Other Baseline Characteristics

Demographics and other baseline characteristics will be summarized descriptively for the ISO Analysis Sets population. A listing will also be provided for this population.

2.3.1 Demographics

Demographics including age and sex will be summarized descriptively.

2.3.2 Other Baseline Characteristics

Baseline characteristics including mode(s) of thermometry consented to by the subject and febrile status will be summarized descriptively.

2.4 Efficacy Analyses

2.4.1 Primary Efficacy Endpoint

The primary efficacy analysis will be carried out on the ISO Analysis Sets (OS, RS, PS, AS). A sensitivity analysis may be performed if any non-compliance that impacts the primary efficacy endpoint is identified.

2.4.1.1 Derivation of Primary Efficacy Endpoint

Clinical accuracy validation will be calculated according to ISO 80601-2-56:2017 + A1:2018. Clinical accuracy includes a measurement of clinical bias, with its limits of agreement, and clinical repeatability[1].

To evaluate the clinical bias for each temperature measurement mode being evaluated (oral, adult axillary, pediatric axillary, and rectal), use the first clinical thermometer under test (DUT) output temperature out of three and the corresponding RCT (Reference Clinical Thermometer) output thermometer from each subject in a test group.

The clinical bias for the specified reference body site and age group is calculated from Formula (2)

$$\Delta_{cb} = \frac{\sum_{i=1}^{n}\left(T_{DUT,i} - T_{RCT,i}\right)}{n} \quad (2)$$

where

i is the index number for an individual subject;

n is the total number of subjects per MEASURING SITE and age group;

$T_{DUT,i}$ is the ith observed OUTPUT TEMPERATURE from the DUT;

$T_{RCT,i}$ is the ith observed OUTPUT TEMPERATURE from the RCT.

To calculate the LIMITS OF AGREEMENT, $\boldsymbol{L_A}$, use Formula (3).

$$\boldsymbol{L_A} = 2 \times \sigma_{\Delta_{cb}} \tag{3}$$

where

$\sigma_{\Delta_{cb}}$ is calculated using Formula (4).

To calculate the deviation, $\sigma_{\Delta_{cb}}$, use the first measurement of the CLINICAL THERMOMETER under test (DUT) OUTPUT TEMPERATURE out of three measurements and the corresponding RCT OUTPUT TEMPERATURE of each subject for the OPERATING MODE being evaluated using Formula (4).

$$\sigma_{\Delta_{cb}} = \sqrt{\frac{\sum_{i=1}^{n}\left[\left(T_{DUT,i} - T_{RCT,i}\right) - \Delta_{cb}\right]^2}{n-1}} \tag{4}$$

where

i is the index number for an individual subject;

n is the total number of subjects per MEASURING SITE and age group;

$T_{DUT,i}$ is the ith OUTPUT TEMPERATURE indicated by the DUT;

$T_{RCT,i}$ is the ith OUTPUT TEMPERATURE indicated by the RCT;

$\boldsymbol{\Delta_{cb}}$ is the CLINICAL BIAS as calculated in Formula (2).

Clinical repeatability is calculated from Formula (5)

An ADJUSTED MODE CLINICAL THERMOMETER that makes continuous estimates of the REFERENCE BODY SITE temperature shall be exempt from the requirements of this subclause.

CLINICAL REPEATABILITY, for a particular OPERATING MODE, is determined for the subject population of all age groups given in Table 201.102 combined. Febrile subjects less than 5 years of age may be excluded.

CLINICAL REPEATABILITY is calculated by a pooled standard deviation of triplicate measurements over the entire population of subjects. First, calculate the standard deviation, σ_j, of the three OUTPUT TEMPERATURE measurements ($T_{1,j}$, $T_{2,j}$ and $T_{3,j}$) for each subject j using Formula (5).

$$\sigma_{j=}\sqrt{\frac{\sum_{i=1}^{m}\left(T_{DUT,i} - \overline{T_{DUT,j}}\right)^2}{m-1}} \tag{5}$$

where

$T_{DUT,i}$ is the *i*th OUTPUT TEMPERATURE (e.g. 1, 2 or 3) indicated by the DUT;

$\overline{T_{DUT,j}}$ is the average of the OUTPUT TEMPERATURES on subject *j*;

m is the number of OUTPUT TEMPERATURE measurements on the subject.

NOTE m is typically equal to 3.

Then calculate a pooled standard deviation (the CLINICAL REPEATABILITY), σ_r, for all subjects using Formula (6).

$$\sigma_r = \sqrt{\frac{\sigma_1^2 + \sigma_2^2 + \ldots + \sigma_j^2 + \ldots + \sigma_N^2}{N}} \quad (6)$$

where

N is the total number of subjects of all age groups in a study.

Definitions:

Clinical Accuracy: closeness of agreement between the output temperature of a clinical thermometer and the true value of the temperature of the reference body site that the clinical thermometer purports to represent

Clinical Bias Δ_{cb}: mean difference between output temperatures of a clinical thermometer and a reference clinical thermometer for the intended reference body site with specified limits of agreement when measured from selected group of subjects

Clinical Repeatability σ_r : pooled standard deviation (over a selected group of subjects, other than febrile subjects less than 5 years old) of changes in multiple output temperatures taken from the same subject from the same measuring site with the same clinical thermometer by the same operator within a relatively short time

Limits of Agreement L_A: the magnitude of a potential disagreement between outputs of two clinical thermometers equal to double the standard deviation of output temperature differences when used on the same human subjects. Limits of agreement can also be described as clinical uncertainty

Monitor (Direct) Mode: operating mode of a clinical thermometer where the output temperature is an unadjusted temperature that represents the temperature of the measuring site to which the probe is coupled

Predictive (Adjusted) Mode: operating mode of a clinical thermometer where the output temperatures are determined by measuring the rate of change of the sensor's output and using that information to anticipate or predict the final equilibrium temperature for the site it is measuring.

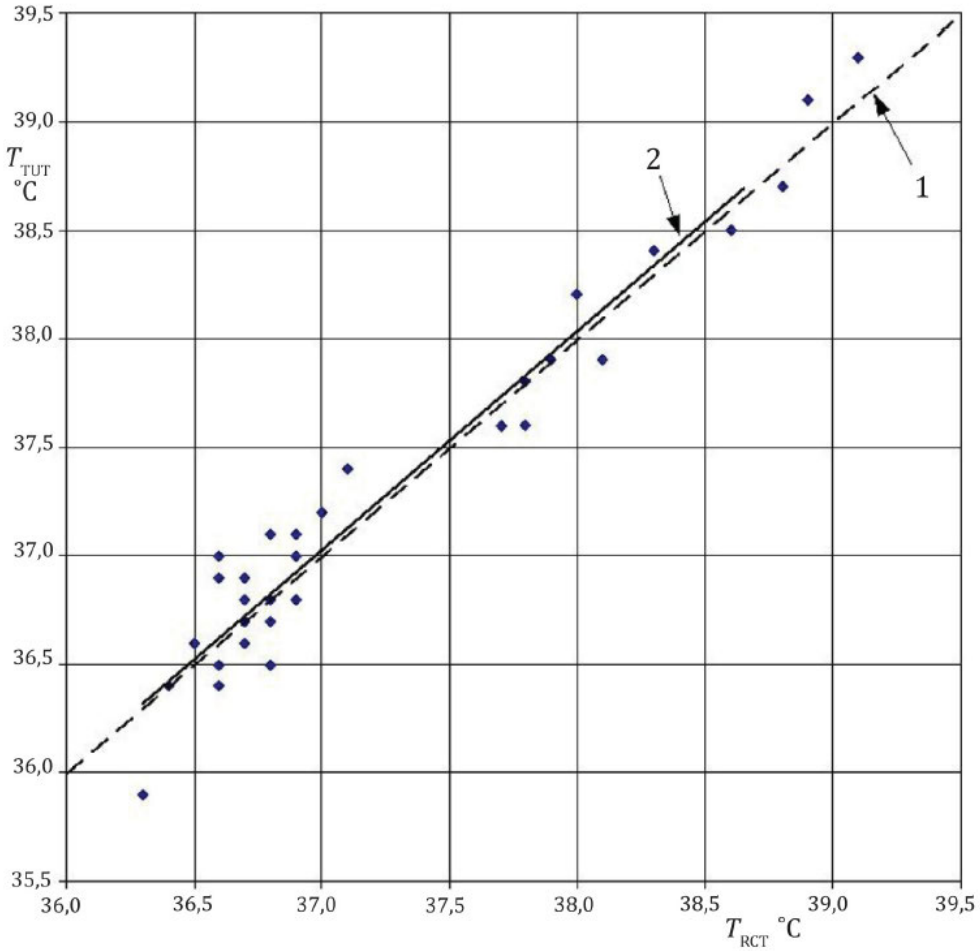
2.4.1.2 Analysis of Primary Efficacy Endpoint

Clinical accuracy will be summarized by clinical bias with its limits of agreement for each reference body site and age group, and by clinical repeatability for each reference body site.

The difference between the first clinical thermometer under test (DUT) output temperature out of three (T_1) and the corresponding RCT output thermometer (T_{RCT}) in a test group will be summarized descriptively by n, mean, standard deviation, median, minimum, and maximum by reference body site and age group.

For each patient, the three sequential output temperatures measured and indicated by a DUT as T_1, T_2 and T_3 will be listed. The standard deviation of the DUT, RCT output temperature (T_{RCT}), and T_1-T_{RCT} for each patient will also be listed.

A comparison plot of T_1 from the DUT and T_{RCT} will be displayed and will include a line of equality and linear regression line[1].



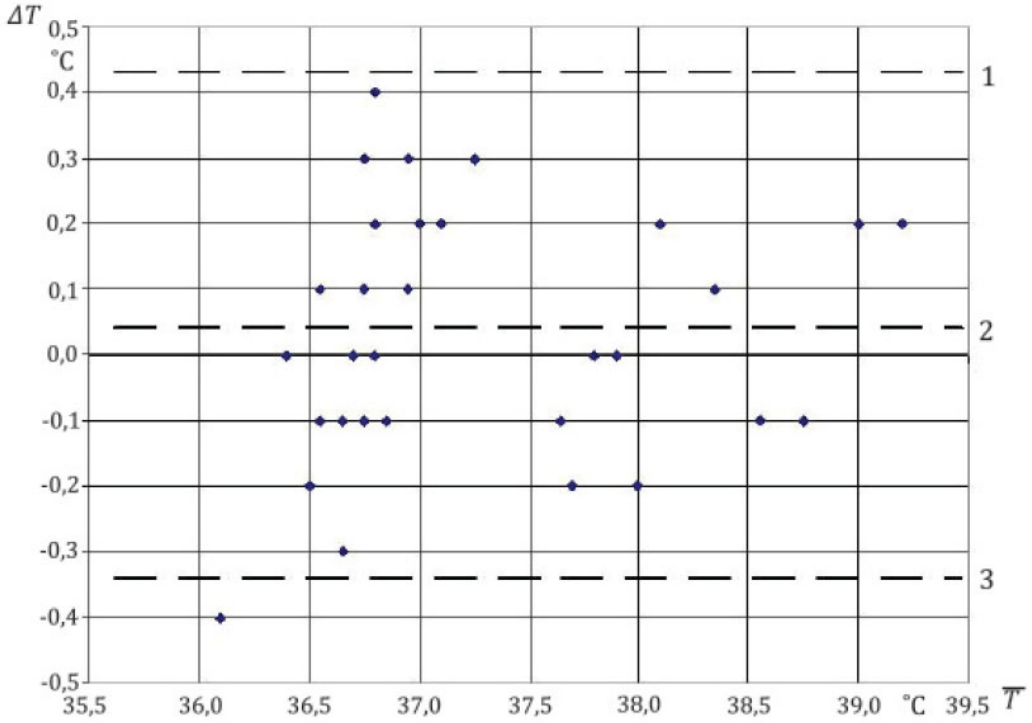
Key

1	line of equality
2	linear regression line
T_{DUT}	is the OUTPUT TEMPERATURE of the DUT
T_{RCT}	is the OUTPUT TEMPERATURE of the RCT

The agreement between T_1 from the DUT and T_{RCT} will be shown using the Bland-Altman method, which will include a Bland-Altman plot. This analysis can only be done on patients who have both T_1 from the DUT and T_{RCT}.

A Bland-Altman Plot will display the temperature difference ($\Delta T = T_1 - T_{RCT}$) versus the average output temperatures of two measurement modes ($\overline{T} = (T_1+T_{RCT})/2$). If the differences are normally distributed, it can be expected that about 95% of them will fall in the range of $\overline{d} \pm 2 \times \sigma_d$. This range is called the "95 % limits of the agreement". Limits of agreement are defined as $2 \times \sigma_d$ per ISO 80601-2-56:2017 + A1:2018. Limits of

agreement characterizes the range within which most differences between the output temperatures by the DUT and the RCT lie[1].



Key

1	$\bar{d} + 2 \times \sigma_d$
2	$\bar{d}$ is the mean difference between OUTPUT TEMPERATURES from the DUT and the RCT
3	$\bar{d} - 2 \times \sigma_d$
ΔT	is the temperature differences between the CLINICAL THERMOMETER under test (DUT) and the RCT
$\bar{T}$	is the average of OUTPUT TEMPERATURES from the DUT and the RCT

2.5 Safety Analyses

All safety analyses will be performed on the SS.

2.5.1 Adverse Event

2.5.1.1 Derivation of Adverse Events

Adverse events (AEs) will be coded using MedDRA. They will be classified as follows:

Treatment-emergent adverse event (TEAE) – An adverse event that starts on or after the start of study treatment

In case of incomplete information on study treatment or AE onset, events will be classified as treatment-emergent unless there is sufficient data to rule out the possibility that the event started after the start of study treatment.

If the severity of an adverse event is missing, then that adverse event will be classified as *severe*.

The number of events per patient will be calculated as follows:

$$\frac{Number\ of\ Total\ Events}{Number\ of\ Patients\ in\ Safety\ Set}$$

2.5.1.2 Analysis of Adverse Events

An AE overview summary table will be prepared to include the number of patients, the percentage of patients (%), the number of events, and the number of events per patient, for the following categories:

1. Any adverse event
2. Any treatment-emergent adverse event (TEAEs)
3. Treatment emergent non-serious AEs
4. Treatment-emergent serious AEs (SAEs)
5. Treatment-emergent study device-related AEs
6. Treatment-emergent study device-related SAEs
7. Treatment-emergent study procedure-related AEs
8. Treatment-emergent study procedure-related SAEs
9. Treatment-emergent AEs leading to withdrawal
10. Treatment-emergent AEs leading to death
11. Any unanticipated adverse device effect (UADE)

Additional tables will be provided by SOC and PT for 2, 5, 7, and 11. Additional listings will be given by SOC and PT for all except 1 and 3. For SAE listings, the seriousness criteria will be included in the listing.

The tables below will display the total number of patients, the percentage of patients (%), the number of events, the number of events per patients, system organ class (SOC), and preferred term. Table summaries will be produced for:

- Treatment-emergent AEs by severity
- Treatment-emergent AEs by relationship to study device
- Treatment-emergent AEs by relationship to study procedure
- Treatment-emergent adverse events in ≥5% of patients

Adverse event listings will be sorted by patient ID, and adverse event start date. They will include primary AE number, SOC, PT, verbatim term, adverse event start date, relationship to study device, relationship to study procedure, severity, action taken, seriousness, outcome, whether the event is ongoing, and whether AE led to discontinuation from study.

2.5.2 Unanticipated Problems

2.5.2.1 Derivation of Unanticipated Problems

Unanticipated Problems will be captured in the eCRF.

2.5.2.2 Analysis of Unanticipated Problems

Unanticipated Problems will be listed.

2.6 Other general principles

2.6.1 Handling of Dropouts or Missing data

All data collected up to the point where the patient drops out will be used for analyses.

2.6.2 Multicenter Studies

This study was conducted in multiple sites across 1 country. Data from all sites will be pooled together for analyses.

2.6.3 Multiple Comparison/Multiplicity

No formal statistical tests are calculated for this study, so no multiplicity adjustments are needed.

2.6.4 Use of an “efficacy subset” of patients

A sensitivity analysis may be performed if any non-compliance that impacts the primary efficacy endpoint is identified.

2.6.5 Rounding and Decimal Places

The estimated mean and median for a set of values will be displayed to 1 more significant digit than the original values, standard deviations will be displayed to 2 more significant digits, and minimum and maximum values will be displayed with the same number of significant digits as the original values. All percentages will be displayed out to 1 decimal place.

3. CHANGES FROM ANALYSIS PLANNED IN PROTOCOL

There are no planned changes in analyses from the protocol.

4. REFERENCES

1. European Committee for Standardization. Medical electrical equipment - Part 2-56: Particular requirements for basic safety and essential performance of clinical thermometers for body temperature measurement. Amendment 1 (ISO 80601-2-56:2017/Amd 1:2018). 2018.

5. APPENDIX

5.1 Appendix 1: List of Tables, Listings, and Figures

This is the list of main tables, listings, and figures for the study. Minor table updates and additions may be done without an update to the SAP, granted they do not change the planned analyses above.

Table Number	Analysis Population	Table Name
14.1.1	N/A	Patient Overview
14.1.2	Enrolled Subjects	Patient Disposition
14.1.3	Enrolled Subjects	Protocol Deviations
14.1.4	ISO Analysis Sets	Demographic and Baseline Characteristics
14.1.5	ISO Analysis Sets	Age Groups by Febrile Status
14.2.1	ISO Analysis Sets	Clinical Accuracy, Clinical Bias and Limits of Agreement
14.2.2	ISO Analysis Sets	Clinical Accuracy, Clinical Repeatability
14.2.3	ISO Analysis Sets	Difference between First DUT Temperature and Corresponding RCT
14.3.1.1.1	SS	Summary of Adverse Events
14.3.1.1.2	SS	Treatment Emergent Adverse Events by SOC and Preferred Term
14.3.1.1.3	SS	Treatment Emergent Adverse Events Related to Study Device by SOC and Preferred Term

14.3.1.1.4	SS	Treatment Emergent Adverse Events Related to Study Procedure by SOC and Preferred Term
14.3.1.1.5	SS	Any Unanticipated Adverse Device Effect by SOC and Preferred Term
14.3.1.1.6	SS	Treatment Emergent Adverse Events in ≥5% of Patients by SOC and Preferred Term
14.3.1.1.7	SS	Treatment Emergent Adverse Events by SOC, Preferred Term and Severity
14.3.1.1.8	SS	Treatment Emergent Adverse Events by SOC, Preferred Term and Relationship with Study Device
14.3.1.1.9	SS	Treatment Emergent Adverse Events by SOC, Preferred Term and Relationship with Study Procedure

Listing Number	**Analysis Population**	**Listing Name**
16.2.1	N/A	Patient Disposition
16.2.2	Enrolled Subjects	Protocol Deviations
16.2.3	N/A	Patients Excluded from Efficacy Analyses
16.2.4	ISO Analysis Sets	Demographic and Baseline Characteristics
16.2.6	ISO Analysis Sets	DUT and Reference Temperature Measurements
16.2.7.1.1	SS	Treatment Emergent Adverse Events
16.2.7.1.2	SS	Treatment Emergent Serious Adverse Events
16.2.7.1.3	SS	Treatment Emergent Adverse Events Related to Study Device
16.2.7.1.4	SS	Treatment Emergent Serious Adverse Events Related to Study Device
16.2.7.1.5	SS	Treatment Emergent Adverse Events Related to Study Procedure
16.2.7.1.6	SS	Treatment Emergent Serious Adverse Events Related to Study Procedure
16.2.7.1.7	SS	Treatment Emergent Adverse Events Leading to Withdrawal
16.2.7.1.8	SS	Treatment Emergent Adverse Events Leading to Death
16.2.7.1.9	SS	Any Unanticipated Adverse Device Effect
16.2.9	Enrolled Subjects	Unanticipated Problem

Figure Number	**Analysis Population**	**Figure Name**

14.2.3.1	ISO Analysis Sets	Comparison of First DUT Temperature and Corresponding RCT
14.2.3.2	ISO Analysis Sets	Bland-Altman Plot of Agreement between First DUT Temperature and RCT