NCT03257189

A Study to Evaluate the Performance, Usability, and Reliability of a Novel Device for Continuous Collection of Physiological Data in Healthcare and Remote Settings

Protocol Number: MC10-PTL-103

Revision 00

Date: June 21, 2017

Investigational Product: BioStamp nPoint

Regulatory Status: Limited to investigational use only

Sponsor: MC10, Inc.
10 Maguire Rd, Bldg. 3
Lexington, MA 02421

This study will be conducted in compliance with the ethical principles of the Declaration of Helsinki (*64th WMA General Assembly, Fortaleza, Brazil October 2013*), ISO 14155:2011, and ICH-GCP Guidelines.

CONFIDENTIALITY STATEMENT

This study is confidential in nature. All information related to this study is considered proprietary and should not be made available to anyone not directly involved in this study. Authorized recipients of this information include investigators and co-investigators, other health care personnel necessary to conduct the study, and the presiding Institutional Review Boards and governing regulatory agencies. The personnel provided with data from this study are hereby informed of its confidential and proprietary nature. Release of these data to individuals other than those listed above requires the prior written permission of MC10, Inc.

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PROTOCOL REVIEW PAGE

STUDY TITLE:	A Study to Evaluate the Performance, Usability, and Reliability of a Novel Device for Continuous Collection of Physiological Data in Healthcare and Remote Settings
PROTOCOL:	MC10-PTL-103
REVISION:	00

Investigator's Statement: I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol; modifications to the study or protocol are acceptable only with a mutually agreed upon protocol amendment. I agree to await IRB approval for the protocol and informed consent before initiating the study, to obtain informed consent from subjects prior to their enrollment in the study, to collect and record data as required by this protocol and case report forms, to prepare annual, final, and adverse effect reports as required by this protocol, and to maintain study documentation for the period of time required.

[redacted]

Sponsor's Statement: I have reviewed and approved this protocol in its entirety and agree to sponsor its implementation.

[redacted]

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Investigator Agreement and Certification

A Study to Evaluate the Performance, Usability, and Reliability of a Novel Device for Continuous Collection of Physiological Data in Healthcare and Remote Settings

I hereby agree to participate in the clinical investigation of the BioStamp nPoint sponsored by MC10, Inc. (hereinafter "Study Sponsor"). I agree to conduct this investigation according to the requirements of the investigational plan provided by the Study Sponsor and in accordance with applicable FDA regulations, ISO 14155:2011, ICH-GCP Guidelines, and in accordance with ethical principles that have their origin in the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil October 2013) and conditions imposed by the reviewing Institutional Review Board (IRB). I agree to ensure appropriate informed consent is obtained from all subjects prior to inclusion in this study.

I understand that the Study Sponsor and/or a designee appointed by Study Sponsor will monitor this investigation. This monitoring will involve periodic inspection of my investigational site and ongoing review of the data that is submitted by me to Study Sponsor. I am also aware that I may be inspected by a representative of the United States Food and Drug Administration (FDA) to verify compliance with applicable federal regulations related to clinical research on human subjects.

I am aware that Study Sponsor reserves the right to discontinue this investigation at any time.

My current curriculum vitae is attached along with the curriculum vitae of those physicians at this institution who will be using this investigational device or participating in this study as co-investigators under my supervision. These include the extent and type of our relevant experience with pertinent dates and locations.

I certify that I have not been involved in an investigation that was terminated for noncompliance at the insistence of Study Sponsor, this institution's IRB/EC or FDA.

I understand that this investigation, protocol, and the trial results are confidential and I agree not to disclose any such information to any person other than a representative of Study Sponsor or FDA without the prior written consent of Study Sponsor.

If requested by Study Sponsor, I will provide financial information, as indicated in 21 CFR 812.43 (c)(5).

Accepted by:

[redacted]

PROTOCOL SYNOPSIS

Title	A Study to Evaluate the Performance, Usability, and Reliability of a Novel System for Continuous Collection of Physiological Data in Healthcare and Remote Settings
Investigational Device	BioStamp nPoint™
Indications for Use	The BioStamp nPoint system is a wireless remote monitoring system intended for use by researchers and healthcare professionals for continuous collection of physiological data in home and healthcare settings. These physiological data include heart rate, heart rate variability, respiration rate, activity (including step count and activity classification), and posture (body position relative to gravity). The system is also intended for measurement of surface electromyography and to monitor limb or body movements during daily living and sleep. Data are transmitted wirelessly from the Sensors for storage and analysis. The device is intended for use on general care patients who are 18 years of age or older as a general patient monitor to provide physiological information. The data from the BioStamp nPoint system are intended for use by researchers and healthcare professionals for research applications or, at the discretion of a qualified healthcare professional, as an aid to diagnosis and treatment. The device is not intended for use on critical care patients.
Study Type	Interventional
Study Phase	Pivotal study for FDA 510(k) submission
Study Objective	The primary objective of the clinical investigation is to: • Evaluate the accuracy of BioStamp nPoint system algorithm measurements and to evaluate the adhesion (reliability) of BioStamp nPoint Sensors.
Study Design	A single-site, non-significant risk, open-label, prospective non-randomized clinical investigation designed to validate the accuracy of the various physiological parameters that the Wearable Sensor Patches acquire and the system processes as well as to validate the performance of the skin adhesive
Enrollment Size	Twenty-five (25) subjects minimally will be enrolled in the study.
Number of Sites	One site in the United States.
Subject Population	Healthy adult subjects will be recruited to participate in this study.
Effectiveness Endpoints	The effectiveness endpoints for this study are the various types of measurements made by the BioStamp nPoint system. All effectiveness endpoints to be statistically summarized will be collected using the BioStamp nPoint and are as follows: • Heart Rate (bpm) • Heart Rate Variability (RMSSD[1] (msec) and LF/HF Ratio[2])

[1] RMSSD: root-mean-square of successive difference of the time intervals between successive heartbeats.

<table>
<tr><td></td><td>

Respiration (average respiration rate)
Activity Classification (activities – sleep, standing, sitting, lying, walking and other)
Activity Parameters - total step counts in a 6 minute walk test
Sleep (sleep onset time (hours, minutes, and seconds), sleep wake time (hours, minutes, and seconds))
Posture Classification (sleep posture, stationary posture standing, stationary posture sitting)

For each endpoint, the BioStamp nPoint measurements will be compared to a similar FDA approved measurement device, other simplistic measurement devices, or to independent observer measurements. The FDA approved measurement devices for this study are the Actiheart heart rate reference device and the Capnostream™ portable respiratory monitor.
<table>
<tr><th>Endpoint Variable Group</th><th>Measurement Comparator</th></tr>
<tr><td>Heart Rate</td><td>Actiheart Device</td></tr>
<tr><td>Heart Rate Variability</td><td>Actiheart Device</td></tr>
<tr><td>Respiration</td><td>Capnostream Device</td></tr>
<tr><td>Activity Classification</td><td>Independent Observer</td></tr>
<tr><td>Activity Parameters</td><td>Manual Step Counting Device</td></tr>
<tr><td>Sleep Parameters</td><td>Independent Observer</td></tr>
<tr><td>Posture</td><td>Independent Observer</td></tr>
</table>
</td></tr>
<tr><td>Data Management</td><td>MC10 sensor and system data to be uploaded to the MC10 cloud by subject and clinical site. MC10 system and reference device to be returned to the clinical site by the subject after completion of protocol activities.

All clinical study source documents to be retained at the site. Copies, where applicable, to be provided to MC10. Reference device data to be downloaded on site and both retained on site and provided to MC10. Any external electronic storage (e.g. DVD) to be retained by the site as source documents.</td></tr>
<tr><td>Safety</td><td>All adverse events (AEs) reported during the evaluation period will be collected and summarized. Serious AEs (SAEs) will be reported in accordance with US Code of Federal Regulation requirements.</td></tr>
<tr><td>Inclusion Criteria</td><td>Subjects must meet all of the following criteria to be eligible for participation in the study:
<u>Inclusion Criteria</u>
1. Male or female volunteers, at least 18 years of age at the time of screening visit;
2. Fluent in English;
3. The subject is willing to comply with the protocol specified evaluations;
4. Subject is willing and cognitively able to sign informed consent</td></tr>
<tr><td>Exclusion Criteria</td><td>Subjects must be excluded from participation in this study if any of the following criteria are met:
<u>Exclusion Criteria</u>
1. Pregnancy;</td></tr>
</table>

[2] LF/HF ratio: the ratio of power in the low-frequency (LF, 0.04-0.15 Hz) and high-frequency (HF, 0.15-0.4 Hz) bands of heart rate variability in the frequency domain.

	2. Positive urine drug screen 3. History of active (clinically significant) skin disorders; 4. History of allergic response to silicones or adhesives; 5. Subjects with electronic implants of any kind (e.g. pacemaker) 6. History of sleep disorders or self-reported insomnia or other sleep conditions; 7. Broken, damaged or irritated skin or rashes near the sensor application sites; 8. Subjects that are MC10 employees or shareholders, or a spouse or child of an MC10 employee or shareholder; 9. Subjects who are physically or cognitively unable to normally perform activities of daily living, assessed at the discretion of the investigator.
Remuneration	Subjects will receive $50 for on-site screening that results in screen fail or enrollment, and a subsequent $1050 for successfully completing the study, where completion is defined as completing the baseline clinic visit, wearing the sensors for two days, returning the sensors to the coordinators, and completing the usability survey.
Study Duration / Follow-up Period	A supervised session which includes one awake and two night-time sleep periods with observation periods throughout; thus a total evaluation duration of approximately 48 hours. One safety and tolerability follow-up call will occur within three to five days post-sensor removal.
Data Analysis Plan	The following analysis populations will be defined for the study: • Intent-to-Measure (ITM) Population – The ITM population will consist of all subjects who are enrolled in the study and for which the ability of each measurement device to measure the subject has been established. • Safety Population – The safety population will consist of all subjects who are enrolled in the study. The ITM population will be the primary analysis set for all effectiveness analyses. The safety population will be used for the analysis of all safety variables and baseline characteristics. For each effectiveness endpoint, the BioStamp nPoint measurements will be compared to the noted comparator device or to independent observer measurements. For pairs of measurements collected on the continuous scale (quantitative to quantitative comparisons), scatter plots with the 45 degree line of agreement superimposed will be constructed from paired observations from the two sources (BioStamp nPoint vs comparator) along with Bland-Altman plots of the data. The mean absolute error (MAE) and the root-mean-square error (RMSE) estimates of agreement will be calculated for each comparison. The standard deviations of each of the agreement measures will also be computed. For pairs of measurements collected on a categorical scale (qualitative to qualitative comparisons), two-way tables of agreement will be constructed for each comparison. The agreement percentage will be computed for each table. The number and percentage of sensor patches in each category of the adhesion

	scoring scale will be tabulated.
ClinicalTrials.gov	Sponsor responsible for study registration per 42 CFR Part 11.
Principal Investigator	[redacted]
Sponsor	MC10, Inc. 10 Maguire Rd, Bldg. 3, First Floor Lexington, MA 02421
Sponsor Contact	[redacted] MC10, Inc. 10 Maguire Rd. Bldg. 3, First Floor Lexington, MA 02421

Table of Contents

List of Figures

List of Tables

LIST OF ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Effect
App	Application - Software
CDER	Center for Drug Evaluation and Research
CRF	Case Report Form
CFR	Code of Federal Regulations
ECG	Electrocardiography
EMG	Electromyography
ES	Enrolled Set
FAS	Full Analysis Set
FDA	Food and Drug Administration
FPFV	First Patient – First Visit
GCP	Good Clinical Practice
HF/LF	Ratio of power in the high-frequency and low-frequency
HR	Heart Rate
HRV	Heart Rate Variability
ICH	International Conference on Harmonization
ICS	Intercostal Space
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
MAE	Mean Absolute Error
MDDS	Medical Device Data System
NSR	Non-Significant Risk
RMSSD	Root-Mean-Square Standard Deviation
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SS	Safety Set
USADE	Unanticipated Serious Adverse Device Effect
WSP	Wearable Sensor Patch

1.0 BACKGROUND AND RATIONALE

Objective and validated assessments of physiological metrics are critical for monitoring data and data trends, and as an aid to assessing disease progression and subsequent therapeutic intervention. In current clinical practice and medical product development, patient historical data, patient-reported outcomes, and in-clinic assessments by physicians are used to evaluate biometrics, but these evaluations are time and context limited and present an incomplete picture of the subject as well as his/her current condition. Some assessments are subjective, or rely on a patient's memory and perception. Other assessments are limited to a specific time interval in a particular environment, like a clinic, preventing accurate longitudinal assessment of fluctuations in physiological parameters. This is particularly true of measurements taken by large stationary clinical instruments, which may limit not only the setting for the measurement but may also affect the subject and change the outcome of the measurement itself.

Wearable sensors have the potential to enable longitudinal, objective monitoring of clinical signs across patient populations, but conventional wearable devices are typically comprised of rigid, packaged electronics, which may compromise overall subject comfort, are often plainly visible when worn in public, and can interfere with activities of daily living and sleep. Finally, emergence of smartphone and wrist-based sensing has led to potential improvements in access and ease of use, but themselves carry limitations in night-time sensing or in creating lower-extremity insight. Consequently, there is a need for assessment tools that are unobtrusive and provide clinical quality, medical grade continuous assessments from multiple body locations.

Conformal, body-worn sensors may provide an easy-to-use and objective alternative. Previously, studies have shown that wearable sensors can be used to provide greater insight into neurological (e.g. Parkinson's disease[1], Huntington's disease[2], multiple sclerosis[3]), sleep[4] (e.g. periodic limb movements, respiration), cardiac monitoring[5] and orthopedics (e.g. physical rehabilitation[6]) movement and biopotential measurements. These studies have demonstrated that data can be collected in an unobtrusive way in remote settings, supporting the possibility of providing more robust, data-based evidence to the clinician and thus to the patient.

The BioStamp nPoint system combines a traditional, electronic platform for collecting Patient Reported Outcomes with multiple, location-agnostic sensors in an adhesive bandage-like form factor. These sensors are flexible enough to conform to the human body and eliminate the profound mismatch in physical properties at the interface between conventional wearable devices and the human body. This new class of soft, conformal electronics and sensors interface better with the surface of the body to minimize discomfort and optimize skin coupling over prolonged use and multiple data-gathering locations. The potential for both in-clinic and remote, longitudinal, multi-sensor, multi-modal, passive and prescribed biometric data tracking is noteworthy.

This first clinical evaluation aims to evaluate the accuracy, reliability, and ease of use of the BioStamp nPoint system as well as the safety, fidelity and tolerability of the BioStamp nPoint Sensors.

2.0 DEVICE DESCRIPTION

The BioStamp nPoint system is a wireless remote monitoring platform intended for use by healthcare professionals and researchers for the continuous collection of physiological data in home and healthcare settings. The system is designed principally for data collection during research studies although may be used wherever and whenever collection of the relevant data is needed.

Figure 1: Illustration of BioStamp nPoint Sensor

The BioStamp nPoint system centers on body-worn Wearable Sensor Patches (“Sensors”, “WSPs”) which can be worn in both in clinic (“supervised”) and remote (“unsupervised”) settings for up to 24 hours at a time, and can be worn repeatedly for multiple days. Study facilitators (either researchers or physicians) set up data collection studies using a web-based study configuration tool, called the Web Portal. For in-clinic uses, the BioStamp nPoint system includes an Investigator Tablet Application that study facilitators use to connect to and configure Sensors. When used at home, study subjects interact with the system through a Mobile Phone Application, the Link App. The Link Hub is used to charge and synchronize data from the Sensors. The BioStamp nPoint system includes an algorithm package that delivers processed metrics on general activity classification, heart rate, heart rate variability, posture, sleep, and respiration during sleep.

2.1 Principles of Operation

When the facilitator configures the study design via the Web Portal, the study configuration is transferred to the Investigator Tablet App (and Link App for remote studies). The Investigator Tablet App and Link App are automatically configured for the specific study design, and when connected to Sensors, configure them per the study design. When user entered data including activity annotations and survey answers are sent from the Investigator Tablet App or Link App, the data travel to an MDDS storage system and are then accessible to facilitators via the Web Portal, which pulls the data from the MDDS storage system. Sensor data is transferred to the MDDS storage through the Link Hub and Link App. If the algorithm package was activated in the study, the algorithm module retrieves the data from the MDDS, processes the data and generates metrics that are returned to the MDDS system for storage. Study facilitators can access all study data (raw and processed) through the Web Portal.

2.2 Indications for Use

The BioStamp nPoint system is a wireless remote monitoring system intended for use by researchers and healthcare professionals for continuous collection of physiological data in home and healthcare settings. These physiological data include heart rate, heart rate variability, respiration rate, activity (including step count and activity classification), and posture (body position relative to gravity). The system is also intended for measurement of surface electromyography and to monitor limb or body movements during daily living and sleep. Data is transmitted wirelessly from the Sensors for storage and analysis.

The device is intended for use on general care patients who are 18 years of age or older as a general patient monitor to provide physiological information. The data from the BioStamp nPoint system are intended for use by researchers and healthcare professionals for research applications or, at the discretion of a qualified healthcare professional, as an aid to diagnosis and treatment. The device is not intended for use on critical care patients.

3.0 STUDY PURPOSE AND OBJECTIVES

The purpose of this pivotal study is to evaluate the performance, usability, and reliability of the BioStamp nPoint system for continuous collection of physiological data in remote (in-home) and healthcare (in-clinic) settings.

The primary objective of the clinical investigation is to evaluate the accuracy of the BioStamp nPoint system algorithm measurements and to evaluate the adhesion (reliability) of the Sensors.

Safety and tolerability will be further assessed via a follow-up telephone call.

4.0 STUDY ENDPOINTS

4.1 Effectiveness Endpoints

The effectiveness endpoints for this study are the various types of measurements made by the BioStamp nPoint system. All effectiveness endpoints to be statistically summarized will be collected using the BioStamp nPoint during in clinic supervised use. The effectiveness endpoints are as follows:

- Heart Rate (bpm)
- Heart Rate Variability (RMSSD[3] (msec) and LF/HF Ratio[4])
- Respiration (average respiration rate)
- Activity Classification (activities – sleep, standing, sitting, lying, walking and other)
- Activity Parameters - total step counts in a 6 minute walk test
- Sleep (sleep onset time (hours, minutes, and seconds), sleep wake time (hours, minutes, and seconds))
- Posture Classification (sleep posture, stationary posture standing, stationary posture sitting)

For each endpoint, the BioStamp nPoint measurements will be compared to a similar FDA-cleared measurement device, other measurement devices, or independent observer measurements. The FDA-cleared measurement devices used as comparators for this study are the Actiheart heart rate reference device and the Capnostream portable respiratory monitor.

Table 1 displays the comparator method for each endpoint category.

Table 1: Endpoint Variable Group and Measurement Comparator

Index	Endpoint Variable Group	Measurement Comparator
1	Heart Rate	Actiheart Device
2	Heart Rate Variability	Actiheart Device
3	Respiration	Capnostream Device
4	Activity Classification	Independent Observer
5	Activity Parameters	Manual Step Counting Device
6	Sleep Parameters	Independent Observer
7	Posture	Independent Observer

[3] RMSSD: root-mean-square of successive difference of the time intervals between successive heartbeats.
[4] LF/HF ratio: the ratio of power in the low-frequency (LF, 0.04-0.15 Hz) and high-frequency (HF, 0.15-0.4 Hz) bands of heart rate variability in the frequency domain.

Individual independent observers will receive training on the operation of all devices and execution of the study protocol before the enrollment of any subjects.

For heart rate and heart rate variability, the values collected will be the one minute average heart rate, the one minute RMSSD and the five-minute LF/HF ratio from the BioStamp nPoint and the one minute average heart rate, RMSSD and five minute LF/HF ratio from the Actiheart device on each of six recording times for each subject. Two readings will be taken while the subject is at rest, two while exercising and two while lying down.

For respiration rate, the average sleep respiration rate values will be collected at one minute time intervals during two separate nights of sleep on each subject using both the BioStamp nPoint and the Capnostream while the subject is asleep.

For the activity classification variable, each subject will be presented with five tasks (standing, sitting, lying, walking and stationary bike riding) in varied order and the activity classification will be recorded by the BioStamp nPoint and by the independent observer. This procedure will be repeated five times for each subject.

For the exercise parameter number of steps taken, the number of steps taken by the subject during a 6 minute walk test will be recorded using both the BioStamp nPoint and a simple step counting device.

For the sleep parameters sleep onset time and wake time, the BioStamp nPoint values and independent observer values will be collected on each night at the study site.

Posture classification variables will be analyzed separately for each type of posture activity (sleep positions, stationary posture standing and stationary posture sitting). For a given posture activity, the posture classification will be recorded by the BioStamp nPoint and the independent observer for two repeats each of each ground-truth posture for each subject. Since sleep position and lying posture are identical, this variable will be assessed from awake subjects to ensure that all postures are represented. Each repeat will generate 5 independent observations of posture. The posture classifications for each posture classification variable are given in Table 2.

Table 2: Posture Variable and Classification

Index	Posture Variable	Posture Classification
1	Sleep positions	Supine, prone, left side and right side
2	Stationary Posture Standing	Upright, lean left, lean right, lean back, lean forward
3	Stationary Posture Sitting	Upright, lean left, lean right, lean back, lean forward

In addition, sensor adhesion to the subject will be measured on a 4 point scale by the independent observer for each of four sensor patches on each subject following 24 hours of continuous wear. The adhesion rating scale (Table 3) is as follows:

Table 3: Sensor Adhesion Rating Scale

Score	Rating	Description
0	= ≥90% adhered	essentially no Sensor lift off the skin
1	= ≥75% to <90% adhered	some edges only of the Sensor lifting off the skin
2	= ≥50% to <75% adhered	less than half of the Sensor lifting off the skin
3	= >0% to <50% adhered but not detached	more than half of the Sensor lifting off the skin without falling off
4	= 0% adhered – Sensor detached	Sensor completely off the skin

Usability will also be assessed by the clinician observing the subject using the system and via a subject questionnaire.

4.2 Safety

All adverse events (AEs) reported during the evaluation period will be collected and summarized. Serious AEs (SAEs) will be reported in accordance with US Code of Federal Regulation requirements.

5.0 STUDY DEVICES

The materials presented in Table 4 are the devices required for the supervised and remote evaluation periods. In addition to the investigational device, a Heart Rate Reference Device and a Respiration Reference Device will be used in this study, and will be applied to the subject as shown in Figure 2. Identification as well as traceability for each investigational and reference device at the study site will be maintained by serial number.

The Actiheart (K052489, CamNtech Inc., Cambridge, UK), used here as the Heart Rate Reference device, is a commercially-available, FDA-cleared, chest-worn monitoring device that records heart rate, Inter-Beat-Interval (IBI), and physical activity. It is designed for calculating and measuring heart rate and Energy Expenditure in free living. The Actiheart has two clips which attach directly to standard ECG electrodes. Usually one electrode is adhered at V1 or V2 (4th intercostal) and the second electrode is placed approximately 10cm away on the left side at V4 or V5, although this placement can be adjusted to be more comfortable for the subject. The number of R-waves detected is recorded, and an internal accelerometer senses the frequency and intensity of the subject's torso movements.

The Capnostream Portable Respiratory Monitor (K150272, Medtronic Inc., Dublin, IE) used here as the Respiration Reference device, is a commercially-available, FDA-approved, bedside, combined capnography/pulse oximetry monitor, capable of providing a complete picture of oxygenation and ventilation by monitoring a subject's:

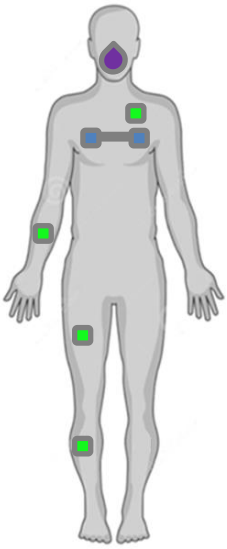
- End tidal carbon dioxide (etCO2) - level of carbon dioxide in exhaled breath.
- Respiratory rate (RR).
- Fractional inspired carbon dioxide (FiCO2) - level of carbon dioxide present during inhalation.
- Oxygen saturation (SpO2).
- Pulse rate (PR).

It is intended to provide professionally trained health care providers the continuous, non-invasive measurement and monitoring of carbon dioxide concentration of the expired and inspired breath and respiration rate, and for the continuous non-invasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO2 and pulse rate).

Additionally, a commercially-available manual "tally" counter will be used for counting steps.

Table 4: Devices for Study Activities

Materials	Purpose	Supervised	Remote
MC10 BioStamp nPoint System			
Sensors	Investigational device	X	X
Link Hub	Investigational device	X	X
Adhesives	Investigational device	X	X
Adhesive Applicator	Investigational device	X	X
Mobile Phone with Link App	Investigational device	X	X
Actiheart (CamNtech Inc.) with electrodes	Reference device: Heart Rate (HR), Heart Rate Variability (HRV)	X	X
Capnostream 35 Portable Respiratory Monitor (Medtronic Inc.) with nasal cannula	Reference device: Respiration Rate	X	-
Manual step counter	Reference device: Step Counting	X	-



	BioStamp nPoint Sensor
	Heart Rate Reference Device
	Respiration Reference Device

Figure 2: Anatomical Locations for Investigational and Reference Devices

6.0 STUDY DESIGN

The study design is a non-significant risk, open-label, prospective non-randomized clinical investigation designed to validate the accuracy of the various physiological parameters that the MC10 Sensors acquire and the system processes, and to validate the performance of the Sensor skin adhesive. The study will be conducted at a single site in the United States.

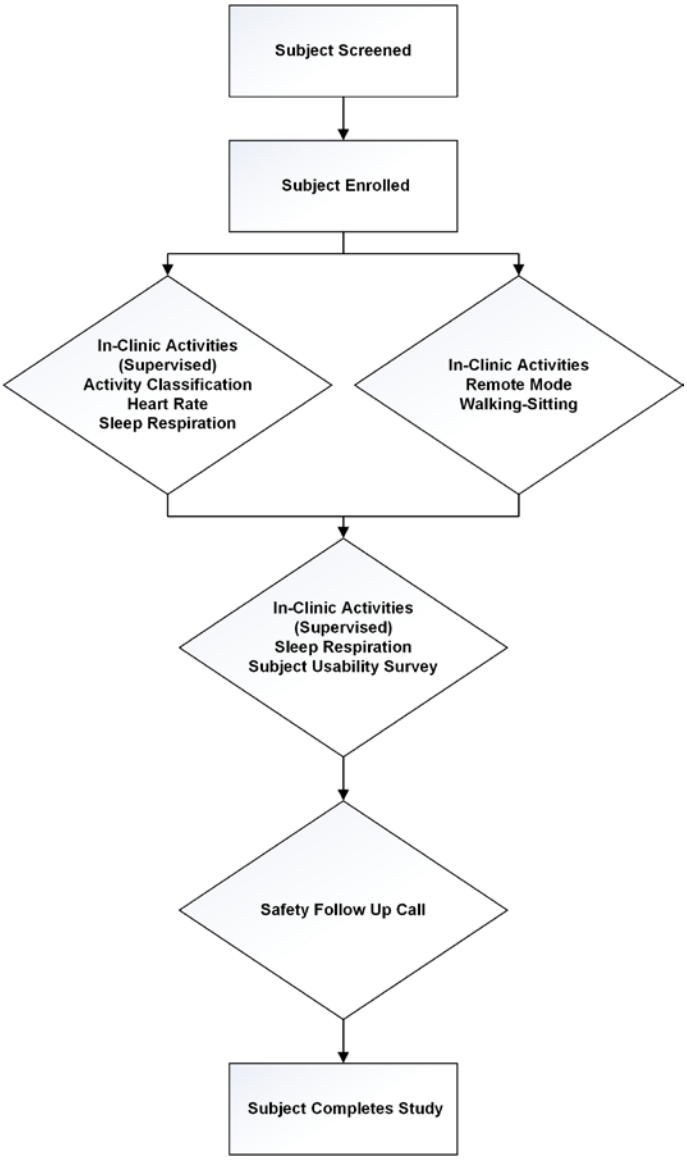


Figure 3: Study Design Flow Chart

6.1 Study Duration

One supervised session of approximately four hours, with observation periods throughout and two night-time sleep periods; thus a total evaluation duration of approximately 48 hours.

At least one safety and tolerability follow-up call will occur within three to five days post-sensor removal.

6.2 Schedule of Events

The evaluation period includes (refer to Section 4.1) clinician observed supervised testing. Subjects will wear a total of four BioStamp nPoint Sensors for this study; chest, thigh, shank, and forearm, and the BioStamp nPoint system will be configured, using only the chest and thigh Sensors, to measure and compute algorithm outputs.
In addition to the algorithm determinate Sensor locations, the shank and forearm Sensors (no sensor data will be collected) will be utilized in combination with the chest and thigh locations to validate the Sensor adhesion performance. The study is designed to capture supervised, observed measurements, as well as two nights of sleep in in clinic supervised setting.

Table 5: Schedule of Events

Activities		Screening Period	Evaluation Period				Safety Follow-Up
			Clinic	Clinic	Clinic	Clinic	
	Visit	1	1 or 2	1 or 2	2 or 3	2 or 3	Telephone
	Day	-60 to 0	0	1	1	2	3-5
Screening & Enrollment Activities							
Informed Consent		X					
Screening survey (demographics, medical history, etc.)		X					
Baseline assessment (weight, Fitzpatrick, medical history, location irritation)		X	X				
Urine pregnancy and drug screen		X	X				
Sensor Application							
Application of Functional MC10 Sensors by Clinician			X				
Application of Non-functional MC10 Sensors by Clinician			X				
Adhesion application assessment			X	X			
Application of Functional MC10 Sensors by Subject				X			
Application of Heart Rate Reference Device by clinician			X				
Application of Respiration Reference Device for Sleep Respiration by clinician			X		X		
Prescribed Activities (Supervised)							
Activity Classification Activities			X				
Heart Rate Activities			X				
Subject training				X			
Overnight sleep			X		X		
Prescribed Activities (Remote)				X			
Time of Removal Assessments (MC10, Heart Rate Reference Device)							
Adhesion assessment				X		X	
Removal pain assessment				X		X	
Skin irritation assessment				X		X	
Sensor Removal							
Removal of Respiration Reference Device for Sleep Respiration by clinician				X		X	
Removal of MC10 Sensors by clinician				X			
Clean MC10 Sensors by clinician				X			
Removal of MC10 Sensors by Subject						X	
Clean MC10 Sensors by Subject						X	
Removal of Heart Rate Reference Device by clinician						X	
Usability Survey				X		X	
Data Transfer							
MC10 Sensor data transfer				X		X	
Respiration Reference Device data transfer				X		X	
Heart Rate Reference Device data transfer						X	
Return sensors to investigators						X	
Safety follow-up call							X
Recording of adverse events			X	X	X	X	X

7.0 STUDY POPULATION

Subjects must meet all inclusion criteria for enrollment in the clinical study and have no exclusion criteria. Reasons for screening failure(s) will be documented.

7.1 Number of Subjects

Minimally, twenty-five (25) healthy subjects (defined as people who do not have the condition or related conditions or symptoms being studied to participate in that study; see also "Accepts Healthy Volunteers" on ClinicalTrials.gov) minimally will be enrolled in the study.

7.1.1 Inclusion Criteria

Subjects must meet all of the following criteria to be eligible for participation in the study:

1. Male or female volunteers, at least 18 years of age at the time of screening visit;
2. Fluent in English;
3. The subject is willing and physically able to comply with the protocol specified evaluations;
4. Subject is willing and is cognitively able to sign informed consent

7.1.2 Exclusion Criteria

Subjects must be excluded from participation in this study if any of the following criteria are met:

1. Pregnancy;
2. Positive urine drug screen
3. History of active (clinically significant) skin disorders;
4. History of allergic response to silicones or adhesives;
5. Subjects with electronic implants of any kind (e.g. pacemaker)
6. History of sleep disorders or self-reported insomnia or other sleep conditions;
7. Broken, damaged or irritated skin or rashes near the sensor application sites;
8. Subjects that are MC10 employees or shareholders, or a spouse or child of an MC10 employee or shareholder;
9. Subjects who are physically or cognitively unable to normally perform activities of daily living, assessed at the discretion of the investigator.

8.0 STUDY PROCEDURES & ASSESSMENTS

The visit schedule, study procedures, and assessments are presented in the Study Design Flow Chart (Figure 3) and the Schedule of Events (Table 5). Site personnel will be instructed via training conducted by MC10 of the investigational device and reference devices protocol specific operation and use and will be documented and approved by MC10 via a verification form.

8.1 Device and System Configuration

Prior to first subject enrollment, for the investigational device, MC10 will design, via the Web Portal, the study activities associated with the BioStamp nPoint system, including appropriate annotation prompts required for execution.

The reference devices and associated software will be configured as necessary to maintain subject traceability and facilitate subsequent data management and analysis. Study site staff will be trained on the proper configuration, application, and use of the reference devices that are presented in Section 5.0 per their associated Instructions for Use as they pertain to the metrics required to fulfil the study objectives.

8.2 Subject Identification

Each subject will be assigned a unique subject number. Subject numbers will not be reassigned or reused for any reason. Only their assigned subject number, initials, and date of birth should identify subjects to the Sponsor. The investigator must maintain a list of potential subjects and enrolled subjects using the Subject Screening/Enrollment Log. At a minimum, this log is faxed (or emailed) to the Sponsor each week. Site will also maintain a Subject ID List in the PI's records ensuring that subjects may be identified in case of product recalls or safety issues.

Any potential subjects who are pre-screened can be added to the log by recording their screening number and initials only. Those who sign the ICF will be assigned a five-digit sequential number. The first two digits will represent the site number (i.e., 01) and the remaining three digits are a sequential patient number (i.e., 001, 002, 003, etc.). Therefore, the fourth subject screened at site number one will be Subject #01004.

8.3 Recruitment

Participants will be recruited via an established database at the clinical site, use of IRB approved flyers and posting on the clinical site website. The completely voluntary nature of participation will be underscored.

8.4 Subject Eligibility, Pre-Screening and Exclusions

Subjects will be asked to participate in this study and will be screened for study eligibility. Each subject will receive an anonymized subject identification number at time of screening that will serve as the subject's identifier throughout the study. A Screening/Enrollment Log will be maintained by the study site, in order to maintain a cumulative tracking of all screened subjects.

8.5 Written Informed Consent

Subjects who pass initial pre-screening will be asked to sign the study-specific Informed Consent form before any study-specific tests or procedures are performed. A member of the research team will inform the potential subject of the elements of the clinical study including, risks, potential benefits and required procedures prior to obtaining the potential subject's informed consent.

8.6 Screening and Baseline (Day 0) Evaluation

The following evaluations are required at the time of subject screening/baseline:

1. Urine pregnancy test and drug screen;
2. Medical History & Current Status – skin disorders;
3. Medical History & Current Status – allergies;
4. Medical History & Current Status – electronic implants;
5. Medical History & Current Status – insomnia/sleep conditions;
6. Evaluation of application sites for broken, damaged, or irritated skin or rashes;
7. MC10 affiliation survey/question
8. Demographics Information: Age, Gender, Height, Weight, Fitzpatrick skin type.

Source documents related to screening activities will be filled out for all screened subjects.

8.7 Subject Enrollment

Subjects who meet all inclusion and none of the exclusion criteria will be considered eligible for enrollment. Subjects will be considered enrolled at Visit 1 prior to application of study devices and measurement capability of the device on the subject has been verified. If the subject does not meet the eligibility criteria at any time before enrollment then the subject will be considered a screen failure. Once enrolled, a subject may only exit the study as a withdrawal (not a screen failure). The reason

for withdrawal will be documented by the investigator on the Study Termination CRF and early termination procedures will be completed for all withdrawn subjects. All records of enrolled but withdrawn subjects will be retained as part of the study.

8.8 Study Assessments – In Clinic – Visit 1 (Supervised)

During the supervised evaluation period, subjects will arrive at the study clinic on Day 0. After admission to the clinic, but before the start of the evaluation period, a skin inspection of planned sensor application sites will be conducted.

The clinical site staff will provision Sensors, a Link Hub, and a Link App phone to the subject using the Link App. They will then apply four Sensors and reference device sensors to the subject. Two of these Sensors will be applied following instructions on the Link App; the other two are for assessing adhesion only, and will be applied following written instructions.

Site staff will then initiate and monitor the prescribed activities for the supervised portion of the study. The prescribed activities consist of general tasks: sitting, standing, lying down, leaning, walking, and biking. The site staff will instruct the subject throughout the evaluation.

For each of the prescribed activities, the site staff will start an annotation in the MC10 Link App to indicate that the subject is starting to perform an activity and will stop the annotation after a specific period of time when the subject has completed the activity. Each annotation will be tagged with a letter and a number. The letter and number used for the annotation of each activity performed will be noted on the CRF. The following activities will be conducted as prescribed in sections 8.8.2 - 8.8.7.

8.8.1 Application of the Heart Rate Reference Device

The Heart Rate Reference Device will be applied as described in Section 5.0, following the manufacturer's IFU, 30 minutes prior to the start of study activities to allow for sensor to body continuity. Heart rate will be monitored throughout the study including during the activities in Table 7 and Table 8.

8.8.2 BioStamp nPoint Sensor Application

The clinician will apply sensors (turned off, no signal data) to the shank and forearm, and functional sensors to the chest, aligned to 60 degrees from the transverse plane with the battery end pointed upwards (left nipple to right shoulder), and thigh, aligned vertically on the central thigh with the battery end pointed upwards, as prescribed by the BioStamp nPoint system IFU. MC10 Sensor adhesion will be assessed (refer to Table 3). The activities in Table 6 will be conducted and annotated following the guided prompts provided by the Link App.

Table 6: Application Activities

Item	Activity	Description	Time	Repetitions
1	Posture Calibration	Subject stands still in an upright vertical position	10 s	1

8.8.3 Activity Classification

The activities in Table 7 will be conducted as prescribed, in a variable order, and will be annotated by the clinician marking the start and stop times for each activity using the Link App. The particular activity performed for a given annotation will be noted on the CRF. This set of activities will be performed 5 times in a random order each time, as listed in the Repetitions column of Table 7.

Table 7: Activity Classification Activities

Item	Activity	Description	Time	Repetitions	Metric
1	Standing Classification	Instruct the subject to stand upright. Once the subject is standing upright, start the activity.	1 min	5	ADL Classifier – Standing HR/HRV – Resting
2	Sitting Classification	Instruct the subject to sit in a chair. Once the subject is sitting, start the activity.	1 min	5	ADL Classifier – Sitting HR/HRV – Resting
3	Lying Classification	Instruct the subject to lie supine. Once the subject is lying in a supine position, start the activity.	1 min	5	ADL Lying HR/HRV – Resting
4	Standing Upright	Instruct the subject to stand against the marked wall, with their right side facing the wall. Instruct the subject to stand upright. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
5	Standing Leaning FRONT	Instruct the subject to stand against the marked wall, with their right side facing the wall. Instruct the subject to lean forward to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
6	Standing Leaning BACK	Instruct the subject to stand against the marked wall, with their right side facing the wall. Instruct the subject to lean back to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
7	Standing Leaning RIGHT	Instruct the subject to stand facing the marked wall. Instruct the subject to lean right to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
8	Standing Leaning LEFT	Instruct the subject to stand facing the marked wall. Instruct the subject to lean left to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
9	Sitting Upright	Instruct the subject to sit in a straight-backed chair. Instruct the subject to sit upright. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
10	Sitting Leaning FRONT	Instruct the subject to sit in a chair. Instruct the subject to lean forward to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
11	Sitting Leaning BACK	Instruct the subject to sit in a chair. Instruct the subject to lean back to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
12	Sitting Leaning RIGHT	Instruct the subject to sit in a chair. Instruct the subject to lean right to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
13	Sitting Leaning LEFT	Instruct the subject to sit in a chair. Instruct the subject to lean left to the 30-degree mark. Once the subject is in position, start the activity.	1 min	5	Posture HR/HRV – Resting
14	Lying SUPINE	Instruct the subject to lie on their back. Once the subject is in position, start the activity.	1 min	5	Sleep posture HR/HRV – Resting
15	Lying PRONE	Instruct the subject to lie flat on their stomach. Once the subject is in position, start the activity.	1 min	5	Sleep posture HR/HRV – Resting
16	Lying RIGHT	Instruct the subject to lie on their right side. Once the subject is in position, start the activity.	1 min	5	Sleep posture HR/HRV – Resting
17	Lying LEFT	Instruct the subject to lie on their left side. Once the subject is in position, start the activity.	1 min	5	Sleep posture HR/HRV – Resting

18	Walking	Instruct the subject to walk for 6 minutes. Once the subject starts walking, start the activity. Count total steps taken by the subject, both legs. Post-activity assessment: How many total steps did the subject take during the walking activity?	6 min	5	ADL Classifier – Walking Pedometer HR/HRV – Moving
19	Walking Classification	Instruct the subject to walk on the treadmill at a constant, comfortable pace. Once the subject starts walking, start the activity.	1 min	5	ADL Classifier – Walking
20	Other Classification	Instruct the subject to bike at a constant, comfortable, low-intensity pace. Once the subject starts biking, start the activity.	8 min	5	ADL Classifier – Other HR/HRV – Moving

8.8.1 Heart Rate Activities

The activities in Table 8 will be conducted as prescribed and will be annotated by the subject marking the start and stop times for each activity using the Link App. The clinician will train the subject on Link App operation and monitor subject performance to ensure that the activities are properly annotated.

Table 8: Heart Rate Activities

Item	Activity	Description	Time (minimum)	Repetitions	Metric
1	Sitting	Sit comfortably in a chair	22 min	At least 2, up to 4	HR/HRV – Resting
2	Walking	Walk on a treadmill at a comfortable pace	22 min	At least 2, up to 4	HR/HRV – Moving
3	Biking	Bike on a recumbent bike at a comfortable pace	22 min	At least 2, up to 4	HR/HRV – Moving

8.8.2 Application of the Respiration Reference Device

The Respiration Reference Device will be applied as prescribed in Section 5.0, following the manufacturer's IFU, prior to the subject going to bed.

8.8.3 Night-Time Sleep Duration

When the subject goes to bed (lights out) and arises from bed (woken by site staff), the sleep onset time and wake time will be recorded by site staff on the CRF. Subjects will be observed throughout the night to annotate on the CRF any periods of wakefulness between these times.

8.8.4 Night-Time Sleep Respiration

Respiration will be captured by the device for the duration of the subject's night of sleep.

8.8.5 Removal of the Respiration Reference Device

The Respiration Reference Device will be removed as prescribed in Section 5.0, following the manufacturer's IFU after the subject arises from bed.

8.8.6 Sensor Adhesion Assessment

On Day 1, prior to removal of the first set of sensors, and after 24 hours of sensor wear for the four body locations, clinical staff will rate the skin adhesion using a 5-point scale (0-4, refer to Table 3)[7] .

Adhesion will be scored by clinical staff based on visual observation and assessment of total unpeeled surface immediately prior to Sensor removal.

8.8.7 Sensor Removal

After at least 24 hours of wear, the clinician will remove Sensors from the chest, thigh, shank, and forearm as prescribed by the BioStamp nPoint system IFU.

8.8.8 Safety and Tolerability Assessment

Safety and tolerability will be assessed immediately by the clinical staff after the Sensor's removal based on qualitative (visual observations) assessments of skin redness.

Skin irritation will be assessed on a 0 to 3 scale based on native assessments (visual observations) of skin irritation using the following scale[8] (Table 9).

Table 9: Irritation Rating Scale

Score	Rating	Description
0	No reaction	---
1	Weakly positive reaction	usually characterized by mild erythema and/or dryness across most of the treatment site
2	Moderately positive reaction	usually distinct erythema or dryness, possibly spreading beyond the treatment site
3	Strongly positive reaction	strong and often spreading erythema with edema and/or eschar formation

8.8.9 Data Download

Site staff will download the data from and recharge the BioStamp nPoint chest and thigh sensors using the Link App. The sensors will not be used again.

Site staff will download the Heart Rate Reference Device data to a dedicated study computer at the end of the wear period using the manufacturer's proprietary software per the instructions for use.

Site staff will download the Respiratory Reference Device data after each night of sleep to a USB stick following the manufacturer's instructions for use.

8.8.10 Subject Training – Remote Kit

The subject will be trained on the BioStamp nPoint system subject IFU and the Link App operations to be performed under observation, defined in Section 8.9. While observed by the clinician, the subject will then apply the sensors to the chest and thigh using the Link App, and will conduct and annotate the activities in Table 8 using the Link App prior to departure from the clinic. The clinician will evaluate adhesion using the scale in Table 3 and observe the subject through re-applying any Sensors with a non-zero score for up to two applications. If two non-zero scores are noted, the clinician should then apply the Sensor.

8.9 Study Assessments – Remote (Unobserved)

After the completion of the supervised evaluation period, subject training, and replacement of BioStamp nPoint sensors on Day 1, the subject will remain in the clinic, where they will continue to wear the BioStamp nPoint system and the Heart Rate Reference Device and execute Table 8 activities.

8.10 Study Assessments – In Clinic – Visit 2 (Supervised)

On the same day (Day 1), the subject will go to bed. Upon waking, clinical site staff will observe the subject removing, cleaning, synchronizing, and beginning to recharge the BioStamp nPoint sensors. Sensor safety and tolerability will then be assessed.

8.10.1 Night-Time Sleep Duration

When the subject goes to bed (lights out) and arises from bed (woken by site staff) the sleep onset time and wake time will be recorded by site staff on the CRF. Subjects will be observed throughout the night to annotate on the CRF any periods of wakefulness between these times

8.10.2 Night-Time Sleep Respiration

When the subject is ready to go to sleep, site staff will place the Respiration Reference Device on the subject as described in Section 5.0, following the manufacturer's IFU. Respiration will be captured by the device for the duration of the subject's night of sleep. After the subject wakes, the Respiration Reference Device will be removed as prescribed in Section 5.0, following the manufacturer's IFU.

8.10.3 Sensor Removal

On the morning of Day 2, while observed by the site staff, the subject will remove sensors from the chest and thigh, and will clean them, synchronize the recorded data, and begin to recharge the sensors as prescribed by the BioStamp nPoint system IFU.

8.10.4 Safety and Tolerability Assessment

Safety and tolerability will be assessed immediately by the clinical staff after the Sensor's removal based on qualitative (visual observations) assessments of skin redness level.

Skin irritation will be assessed on a 0 to 3 scale based on native assessments (visual observations) of the skin sensor locations using the scale[9] located in Table 9.

8.10.5 Equipment Return

The Heart Rate Reference Device will be removed. The subjects will return the provisioned equipment; equipment return will be documented on the Device Accountability Form.

8.10.6 Usability Survey

Subjects will complete a survey related to the intuitiveness and ease of use of the BioStamp nPoint system.

8.11 Data Download

The clinical staff will verify that the data from the BioStamp nPoint system has successfully been uploaded to the BioStamp nPoint cloud, and will download the data from the Heart Rate Reference Device and the Respiration Reference Device after the system is returned on Day 2. Algorithm outputs will be derived from the Web Portal.

8.12 Subject Follow-up

A Safety follow-up telephone call will be made between Day 3 and Day 5 to assess for adverse events associated with study participation.

9.0 Completion or Early Withdrawal of Subjects

9.1 Subject Completion

Completion of the study is defined as:

1. completing the supervised activities;
2. wearing the sensors for two days;
3. returning the sensors to the coordinators;
4. completing the usability survey;
5. completing the follow-up telephone call.

9.2 Subject Early Discontinuation / Withdrawal of Subjects

Subjects are free to withdraw from the study at any time, without prejudice. Subjects should be withdrawn from the study if any of the following events occur:

1. Subject develops an illness or any other condition or event that would interfere with his/her continued participation;
2. Subject is noncompliant with the study procedures, or unable to continue in the opinion of the Investigator;
3. Subject withdraws his/her consent;
4. The Sponsor or a regulatory agency requests withdrawal of the subject.

Investigators should attempt to obtain information on subjects, in the case of withdrawal or discontinuation. For subjects considered as lost to follow-up, the Investigator should make an effort (at least 1 phone call to the subject on each of 2 separate days), and document his/her effort (date and summary of the phone call in the source documents) to complete the final evaluation. All results of these evaluations and observations, together with a narrative description of the reason(s) for discontinuing the subject, must be recorded in the source documents. The Study Termination Case Report Form (CRF) must document the primary reason for withdrawal or discontinuation.

10.0 Risk / Benefit Analysis

10.1 Benefits

There are no direct benefits for the subjects participating in this study. However, the knowledge gained from this study may be important for improving short and long - term patient monitoring and providing subjective data, both in the clinic and remotely, for capturing physiological metrics that may aid researchers and healthcare professionals.

10.2 Risks

The risks of the investigational procedure to subjects are expected to be minimal under this protocol and are described in Section 14.5.

The BioStamp nPoint system sensor includes a non-invasive biosensor that is attached to the surface of the skin using an adhesive sticker, and is designed to measure movement, heart rate, heart rate variability, and sleep metrics using embedded accelerometer, gyroscope, and electrodes. The study is designed to assess the system's ability to capture and analyze movement, heart rate, heart rate variability, and sleep.

This is the first clinical trial for this device. The study will enroll healthy subjects at one study site in the United States.

The device will not be used in this study as an implant; it will not be used to support or sustain human life; it will not be of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health in this study; and the use in this study will not otherwise present a potential for serious risk to the health, safety, or welfare of a subject. Harm

resulting from use of the device is not considered a serious risk. In addition, no other study procedures will be performed that would place the subjects at significant risk. As indicated in Section 14.5, skin irritation is an anticipated risk.

The BioStamp nPoint system is Non-Significant Risk under the proposed investigational study based on a comprehensive risk analysis per Investigational Device Exemptions, 21 C.F.R. § 812.3(m) (2016) and proposed use of the device[10].

10.3 Minimization of Risk and Monitoring Procedures

MC10 has attempted to mitigate risks as much as possible through product design, testing, and through careful labeling and instructions for use. Risks will be further mitigated through selection of qualified physicians, appropriate training, and study monitoring ensured by the following:

- Investigators who participate in the study will be experienced and skilled in collection of physiological data. Additionally, investigators, in conjunction with the investigational site, will have adequate resources for participation in a clinical study.
- Each investigator will ensure oversight and approval of the study by an Institutional Review Board (IRB) prior to initiation of the clinical study at his/her investigational site.
- The investigator and study personnel will be trained on the clinical protocol, investigational device and Instructions for Use.
- Subjects will be carefully evaluated against the inclusion/exclusion criteria prior to entering the clinical study to ensure that their diagnosis and medical status are appropriate for participation in the clinical study.
- Subjects will be monitored throughout the follow-up period as defined in the study protocol.
- Any adverse events occurring during the time of the investigational procedure will be closely monitored and the subject shall be followed until resolution or is judged to be chronically stable, and any deleterious trends investigated as early as possible.

11.0 STATISTICAL METHODS

11.1 Introduction

The study is a non-significant risk, prospective, non-randomized study of the performance characteristics of the BioStamp nPoint device in healthy adult subjects. Subjects will be enrolled in the trial for approximately 48 hours. The primary objectives of the statistical analyses are to evaluate the agreement of the BioStamp nPoint measurements to commonly accepted measurement standards.

A study center is defined as a hospital or medical office under the control and supervision of the Principal Investigator.

11.2 Sample Size

The sample size of n=25 subjects is sufficient to meet business needs of the Sponsor and is comparable to the size of studies with similar devices. An additional 5 subjects may be enrolled to account for a 20% dropout rate.

11.3 Effectiveness Variables

The effectiveness endpoints for this study are the various types of measurements made by the BioStamp nPoint system. All effectiveness endpoints to be statistically summarized will be collected using the BioStamp nPoint during the supervised-use phase. The effectiveness endpoints are as follows:

- Heart Rate (bpm)
- Heart Rate Variability (RMSSD[5] (msec) and LF/HF Ratio[6])
- Respiration (average respiration rate)
- Activity Classification (activities – standing, sitting, lying, walking and other)
- Activity Parameters - total step counts in a 6 minute walk test
- Sleep (sleep onset time (hours, minutes, and seconds), sleep wake time (hours, minutes, and seconds))
- Posture Classification (sleep posture, stationary posture standing, stationary posture sitting)

For each endpoint, the BioStamp nPoint measurements will be compared to a similar FDA approved measurement device, to other basic or manual measurement devices, or to independent observer measurements. The FDA approved measurement devices for this study are the Actiheart heart rate reference device and the Capnostream portable respiratory monitor. Table 10 displays the comparator method for each endpoint category.

Table 10: Endpoint Variable Group and Measurement Comparator

Index	Endpoint Variable Group	Measurement Comparator
1	Heart Rate	Actiheart Device
2	Heart Rate Variability	Actiheart Device
3	Respiration	Capnostream Device
4	Activity Classification	Independent Observer
5	Activity Parameters	Manual Step Counting Device
6	Sleep Parameters	Independent Observer
7	Posture	Independent Observer

Individual independent observers will receive training on the operation of all devices and execution of the study protocol before the enrollment of any subjects.

For heart rate and heart rate variability, the values collected will be the one minute average heart rate, the one minute RMSSD, and the five-minute LF/HF ratio from the BioStamp nPoint and the one minute average heart rate, the one minute RMSSD, and five minute LF/HF from the Actiheart device on each of six recording times for each subject. Two readings will be taken while the subject is at rest, two while exercising and two while lying down. These readings will be collected during the activities listed in Table 7 and Table 8.

For respiration rate, the average resting respiration rate values will be collected at one minute time intervals during sleep on each subject using both the BioStamp nPoint and the Respiration Reference Device.

For the activity classification variable, each subject will be presented with five tasks (standing, sitting, lying, walking and stationary bike riding) in varied order and the activity classification will be recorded by the BioStamp nPoint and by the independent observer. This procedure will be repeated five times for each subject.

[5] RMSSD: root-mean-square of successive difference of the time intervals between successive heartbeats.

[6] LF/HF ratio: the ratio of power in the low-frequency (LF, 0.04-0.15 Hz) and high-frequency (HF, 0.15-0.4 Hz) bands of heart rate variability in the frequency domain.

For the exercise parameter “number of steps taken”, the number of steps taken by the subject during a 6 minute walk test will be recorded using both the BioStamp nPoint and a simple step counting device. This procedure will be repeated five times for each subject.

For the sleep parameters sleep onset time and wake time, the BioStamp nPoint values and independent observer values will be collected on each night and morning at the study site.

Posture classification variables will be analyzed separately for each type of posture activity (sleep positions, stationary posture standing and stationary posture sitting). For a given posture activity, the posture classification will be recorded by the BioStamp nPoint and the independent observer for two repeats each of each ground-truth posture for each subject. Each repeat will generate 5 independent observations of posture. The posture classifications for each posture classification variable are given in Table 11.

Table 11: Posture Variable vs Classification

Index	Posture Variable	Posture Classification
1	Simulated sleep positions	Supine, prone, left side and right side
2	Stationary Posture Standing	Upright, lean left, lean right, lean back, lean forward
3	Stationary Posture Sitting	Upright, lean left, lean right, lean back, lean forward

Sensor adhesion to the subject will be measured on a 4 point scale by the independent observer for each of four sensor patches on each subject following 24 hours of continuous wear. The adhesion rating scale is presented in Table 3.

11.4 Analysis Populations

The following analysis populations will be defined for the study:

- Intent-to-Measure (ITM) Population – The ITM population will consist of all subjects who are enrolled in the study and for which the ability of each measurement device to measure the subject has been established.

- Safety Population – The safety population will consist of all subjects who are enrolled in the study.

The ITM population will be the primary analysis set for all effectiveness analyses. The safety population will be used for the analysis of all safety variables and baseline characteristics.

11.5 Analysis Subgroups

There is no subgroup analysis planned for the study.

11.6 Statistical and Analytical Plans

11.6.1 Disposition and Demographics

A table will be constructed with counts and percentages of the number of subjects who were screen failures, the number of subjects enrolled in the study, the number of subjects withdrawn from the study before study completion, and the number who completed the study. For those subjects who withdrew before completion of the study, counts and percentages of the reasons for withdrawal will be tabulated.

The continuous demographic characteristics at screening will be summarized for all subjects in the safety population using descriptive statistics (mean, standard deviation, median, minimum, maximum, and number of non-missing observations). The categorical baseline characteristics will be summarized for the safety population using frequency counts and percentages.

11.6.2 Effectiveness Endpoint Analyses

For pairs of measurements collected on the continuous scale (quantitative to quantitative comparisons), scatter plots with the 45 degree line of agreement superimposed will be constructed from paired observations from the two sources (BioStamp nPoint vs comparator) along with Bland-Altman plots of the data. The mean absolute error (MAE) and the root-mean-square error (RMSE) estimates of agreement will be calculated for each comparison. The standard deviations of each of the agreement measures will also be computed.

For pairs of measurements collected on a categorical scale (qualitative to qualitative comparisons), two-way tables of agreement will be constructed for each comparison. The agreement percentage will be computed for each table.

The number and percentage of sensor patches in each category of the adhesion scoring scale will be tabulated.

The statistical analyses of the effectiveness data will also be described in the Statistical Analysis Plan (SAP) for the study. The SAP will be written and finalized prior to database lock.

11.6.3 Safety Analysis

Prior to analysis, all AEs will be coded using the MedDRA coding dictionary. Based on these coded terms, TEAEs will be summarized using system organ class and preferred terms, as well as by relationship to the study devices. All AEs will be listed, regardless of whether or not they were study treatment related.

11.7 Handling Missing Data

In the statistical analysis of the primary effectiveness endpoints of the study, only the time points for each subject with evaluable endpoints for the both the BioStamp nPoint and the comparator method will be used in the statistical analysis, i.e., a complete case analysis. The handling of missing values for all other study endpoints will be described in the SAP for the study.

11.8 Interim Analysis

There are no interim analyses planned for this study.

12.0 DATA MANAGEMENT

12.1 Data Flow

Data generated by the BioStamp nPoint system and the reference devices, as well as data annotated on the CRFs, will be extracted and time-aligned by MC10 for entry into the trial database. During study execution, ground-truth data collected on CRFs and by reference devices will be stored at the study site. Data collected using BioStamp nPoint will be transmitted to the MC10 Cloud for processing and generation of analytic outputs. The process described below allows verification that the extraction and time-alignment processes do not introduce changes in the underlying data.

After the final subject has completed the study, the sum total of analytic outputs from the study will be exported from the MC10 Cloud and stored in a read-only archive. This archive will be entered into

MC10's Quality system, and a checksum to uniquely represent this archive will be computed. This checksum will be sent for entry into the trial database. After the checksum has been entered, CTI will archive all ground-truth data in a read-only format and compute a checksum on the resulting archive. This checksum will also be entered into the trial database. CTI will then send the ground-truth data archive to MC10 for data extraction and time-alignment. MC10 will then send the relevant data for entry into the trial database and subsequent analysis. All tools to be used in this process will be validated.

12.2 Data Collection

Data management will be performed by MC10 or their designee using a validated data system as specified in 21 CFR 11. Subject data will be entered into CRFs and combined with data provided from other sources in a validated data system that will reside in the clinical data management database.

Clinical data management will be performed in accordance with applicable MC10 or their designee's SOPs; data cleaning procedures will be performed with the objective of ensuring all data fields are populated, and removing errors and inconsistencies in the data which would otherwise impact the analysis and reporting objectives, or the credibility of the final study report.

The principal investigator is responsible for the accuracy and completeness of all study documentation. The clinical monitor will collect the originals and the investigational site shall retain the copies.

12.3 Data Processing

Visual and computer error checks will be carried out. The investigator will be queried on errors concerning completeness and consistency. Audits may be performed for quality assurance of data handling.

13.0 MONITORING AND QUALITY CONTROL PROCEDURES

13.1 Monitoring and Auditing

Sponsor personnel or their designees will monitor the study and verify subject data and ensure compliance with Good Clinical Practice (GCP), clinical protocol and other study requirements. Monitoring visits to the clinical site(s) will be made periodically during the study, to ensure that all aspects of the current, approved protocol/amendment(s) are followed.

Prior to the enrollment of any subject in this study, the Monitor and the Investigator will review the protocol, the procedure for obtaining informed consent and the procedure for reporting adverse events. On-site and remote monitoring visits will be performed by the Monitor. Case report forms will be verified against source documentation and subject compliance will be monitored.

The Monitor is responsible for ensuring, through personal contact with the Investigator and site personnel that the members of the clinical staff clearly understand and accept the obligations incurred in this investigation, and that these obligations are being fulfilled throughout the study. Specifically, the Monitor will interact with the site via telephone contact and periodic on-site visits to ensure that:

- Study facilities continue to be acceptable for the conduct of the study
- Regulatory and study documents are complete and up-to-date
- The protocol is appropriately followed
- Protocol amendments have been approved by the IRB and the local regulatory authorities (as applicable), and the Sponsor has received the approval in writing
- Qualified subjects are enrolled in a timely manner
- Accurate, complete, and current records are maintained for all subjects

- The information recorded and submitted to the Sponsor is representative of the subject record and other supporting documentation
- Problems with inconsistent and incomplete data are addressed
- Accurate, complete, and timely adverse event reports are being made to the Sponsor
- The Principal Investigator continues to assume primary responsibility for the study
- Investigational devices are properly stored, dispensed, and accounted for

13.2 Device Labeling

Labeling for the investigational devices will be limited to product labels and the Instructions for Use (IFU) for the operation of the device. The packaging of the BioStamp nPoint system will be labeled in compliance with 21 CFR Part 812.5. Each device label will include the wording "Caution – Investigational Device. Limited to Investigational Use" or similar language.

13.3 Device Accountability

Access to investigational devices shall be controlled and used only in the clinical investigation and according to the Protocol.

The Sponsor shall keep records to document the physical location of all investigational devices from shipment (or hand-carried) to the sites until return or disposal.

The principal investigator or an authorized designee shall keep records documenting the receipt, use, return, and disposal of the investigational device, which shall include:

- The date of receipt
- Identification of each investigational device (serial and or lot number)
- The date or dates of use
- Subject identification
- Date of return of unused, expired, or malfunctioning investigational device, if applicable

The Investigator must explain in writing the reasons for any discrepancy noted in device accountability.

14.0 ADVERSE EVENTS

14.1 Definitions

Adverse events will be recorded and documented throughout the duration of the study. In this study, adverse events will be defined and classified per ISO 14155:2011(E) Clinical Investigations of Medical Devices in Human Subjects - Good Clinical Practice and all applicable internal Sponsor procedures; see Table 12 for details. Per ISO 14155:2011(F), "ADE" will include any AE related to the investigational device, as well as any AE related to study design.

Table 12: Adverse Event Definitions

<table>
<tr><th>Adverse Event</th><th>Non-device related</th><th colspan="2">Device- or procedure-related</th></tr>
<tr><td>Non-serious</td><td>Adverse Event</td><td colspan="2">Adverse Device Effect (ADE)</td></tr>
<tr><td rowspan="3">Serious</td><td rowspan="3">Serious Adverse Event</td><td colspan="2">Serious Adverse Device Effect (SADE)</td></tr>
<tr><td>Anticipated</td><td>Unanticipated</td></tr>
<tr><td>Anticipated Serious Adverse Device Effect</td><td>Unanticipated Serious Adverse Device Effect</td></tr>
</table>

14.1.1 Adverse Events

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

All adverse events, regardless of relationship to the device, must be recorded, as applicable, on the case report forms provided. Adverse events that occur during this study should be treated by established standards of care, which will protect the life and safety of the subjects.

Adverse events shall be assessed and documented at the time of the procedure and at all study follow-up visits. Each investigator shall provide source documentation as requested by the Sponsor to facilitate reporting and adjudication of these events.

14.1.2 Serious Adverse Events

An adverse event is considered a Serious Adverse Event (SAE) that

a. led to death

b. led to a serious deterioration in the health of the subject, that either resulted in

1) a life-threatening illness or injury, or

2) a permanent impairment of a body structure or a body function, or

3) in - patient hospitalization or prolongation of existing hospitalization, or

4) a medical or surgical intervention to prevent permanent life-threatening illness or injury or permanent impairment to body structure or a body function.

c. led to fetal distress, fetal death or a congenital abnormality

14.1.3 Unanticipated Serious Adverse Device Effect

An Unanticipated Serious Adverse Device Effect (USADE) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death were not previously identified in nature, severity, or degree of incidence in the investigational plan or labeling, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

14.2 Adverse Event Reporting

Any adverse event that occurs during the course of the study must be reported using the appropriate form in the CRFs and the Investigator must sign each report. The Investigator must determine whether the adverse event is serious or unanticipated, its intensity, and the relationship of each adverse event to the investigational devices.

All serious adverse events, including unanticipated serious adverse device effects, must be reported within 24 hours of the site first becoming aware of the event using the appropriate CRF. All other adverse events (i.e. other than serious adverse events or unanticipated adverse device effects) must be recorded on the appropriate CRFs. The Medical Monitor will contact the site for additional information, if required.

For any adverse event that is ongoing at the time of the initial report, periodic follow-up information is required until the adverse event is resolved or is judged to be chronically stable. The site should submit relevant follow-up information related to the adverse event as soon as it is available.

Depending upon the nature and seriousness of the adverse event, the Medical Monitor may request the Investigator to provide copies of the subject's medical records (such as the subject's laboratory tests and hospital records, Investigator summaries, etc.) to document the adverse event. The Medical Monitor is available to respond to any medical issues that arise during the conduct of this

study.

The Investigator will report all serious adverse events, including unanticipated adverse device effects, to the IRB according to the IRB requirements. A copy of this IRB communication should be sent to the Sponsor.

Within 10 working days of notification, the Sponsor will report all unanticipated adverse device effects to the appropriate authority, all participating investigators, and all reviewing IRB. The Sponsor will ensure that safety reporting for the study is conducted in compliance with all pertinent requirements and regulations.

14.3 Adverse Event Reporting

14.3.1 Initial Assessment

The investigator must provide the following information:

- Date of onset
- Nature
- Severity
- Duration / date of resolution
- Outcome
- Relationship to investigational device
- Other relevant information

14.3.2 Assessment of Severity

The Investigator must determine the severity of the adverse event according to the following definitions:

- **Mild -** The adverse event is noticeable to the subject, but does not interfere with routine activity; the symptoms are easily tolerated and transient in nature.
- **Moderate** – The adverse event interferes with routine activity but responds to symptomatic therapy or rest; the symptoms are poorly tolerated and sustained.
- **Severe** – The adverse event significantly limits the subject's ability to perform routine activities despite symptomatic therapy. The adverse event requires medical or surgical treatment or results in hospitalization.
- **Life-Threatening – The subject is at immediate risk of death.**

14.3.3 Device Relatedness

The Investigator must provide an assessment of the adverse event association of device relatedness according to the following definitions:

- **Definite** – The adverse event is clearly related to the investigational device: the event has a temporal relationship to the investigational device, follows a known pattern of response, or is otherwise logically related to the investigational device, and no alternative cause is present.
- **Probable (Likely)** – The adverse event is likely related to the investigational device: the event has a temporal relationship to the investigational device, follows a known or suspected pattern of response, or is otherwise logically related to the investigational device, but an alternative cause may be present.
- **Possible (Unlikely)** – The adverse event is unlikely related to the investigational device: the event does not follow a clear temporal relationship to the investigational device or

does not follow a known pattern of response, or is otherwise likely to be due to the subject's clinical state or other modes of therapy.

- **Not Related** – The adverse event is clearly not related to the investigational device: the event has no temporal or other relationship to the administration of the investigational device follows no known or suspected pattern of response, and an alternative cause is present.
- **Unknown** – Unable to determine the relationship based on all available information.

14.4 Device Deficiency

A Device Deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance (includes malfunctions, use errors, and inadequate labeling). Sponsor will assess all device deficiencies that could have led to a serious adverse device effect for potential regulatory reporting requirements.

In the event of a suspected malfunction or device deficiency, the investigational device shall be returned to the Sponsor for analysis. Instructions for returning the investigational device will be provided by the sponsor.

14.5 Anticipated Device Related Effects

As a dermal application, the BioStamp nPoint sensors may cause mild skin irritation/reactions; however, these reactions can be moderate to severe. These skin reactions (such as macular erythema, allergic reactions, inflammation, pain, skin irritation/damage) are expected to be minor because the patient contact material of the BioStamp nPoint was specifically selected based on its biocompatibility. However, these skin reactions may manifest to a more severe form (such as burning, blistering, and intense redness). If an anticipated device related effect manifests in an uncharacteristic or unusual manner (e.g., an effect occurs with greater severity or specificity from that mentioned above), the effect should no longer be considered anticipated.

Any anticipated device effect that results in a SAE or SADE must be reported to MC10 in accordance with the procedures outlined in Section 14.3.

15.0 MEDICAL MONITORING

The principal investigator will review adverse event reports as they arise and be responsible for determining whether to alter or stop a subject's participation. Subjects are instructed to report any adverse effects or concerns immediately; in addition, we will directly inquire as to adverse events at the exit interview. Subjects are free to terminate participation in the study at any time. No formal Data Safety Monitoring Board is planned.

Adverse events and unanticipated problems involving risks to subjects or others will be reviewed by the principal investigator, who will judge whether event(s) were expected or not, or related or not to the study. In addition, the investigator will also determine the best course of action to ensure subject safety.

MC10 will be responsible for receiving SAE reports from the study site, gathering information from the study site concerning these Serious Adverse Events, reporting these SAEs to FDA on the proper forms within the time constraints specified in the CFR, and following up with the study site until the SAE resolves.

16.0 STUDY ADMINISTRATION

16.1 Statement of Compliance

The clinical investigations will be in accordance with the ethical principles of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil October 2013), ISO 14155:2011 and ICH-GCP Guidelines.

- The clinical investigation shall not commence until approval by the IRB.
- Any additional requirements imposed by the IRB or regulatory authority shall be followed.
- The Sponsor shall maintain a Clinical Trial Liability Policy with an insurance company.

16.2 IRB Approval

The study protocol shall be reviewed and approved by the investigator's IRB or a contract IRB if the participating institution allows, prior to subject enrollment. The Sponsor must review any proposed changes to the investigational plan prior to implementation. The Sponsor and the IRB must approve significant changes to the investigational plan in writing by prior to implementation. A significant change is one which may increase the risk or present a new risk to a subject, or which may adversely affect the scientific validity of the study.

Prior to shipment of investigational devices, a signed copy of the IRB approval letter identifying the clinical study and investigational site is required to be submitted to the Sponsor. Investigators are responsible for obtaining and maintaining annual renewal of the study by their IRB (or according to renewal schedule imposed by the IRB). Evidence of renewal and continued IRB approval must be provided to the Sponsor accordingly.

16.3 Informed Consent

Informed consent is mandatory and must be obtained from all subjects as per local regulations, prior to their participation in the study.

It is the responsibility of the Investigator to ensure that written informed consent from each subject, or the legally authorized representative of the subject, is obtained prior to the initiation of any study-related procedures.

Subjects who agree to participate in this study will do so voluntarily. They will be treated on an equal basis with all other subjects.

Study personnel fully knowledgeable in the purposes and procedures of the study will approach all prospective study participants. The facilities and settings in which prospective participants will be presented with the opportunity to learn about and consent to participation in the study will provide them sufficient quiet and unhurried time to be informed of the study, to ask questions, and between consent being given and the initiation of study procedures. Study personnel will, after presenting the study to prospective participants, assess the subject's understanding and autonomy by asking the subject to explain the study in his/her own words.

Once that step is completed, consent will be able to be given by the subject's signing the consent form. A copy of the consent form will be given to all consented participants.

Signed subject consent forms must be retained in the study files by the Investigator, and available for review by the Sponsor and/or regulatory agencies, as applicable.

The informed consent form and any other written information provided to subjects will be revised whenever important new information becomes available, or if there is an amendment to the protocol which necessitates a change to the content of subject information and/or to the consent form. The Investigator will inform the subject of changes in a timely manner, and will ask the subject to confirm his/her continuation in the study by signing a revised consent form.

Any revised informed consent form and other written information provided to subjects must receive IRB, Sponsor, and regulatory agency approval, as applicable.

16.4 Amending the Protocol

This protocol is to be followed exactly, and will only be altered by written amendments. Amendments must be approved by all parties responsible for approving the Protocol including the IRB prior to implementation. However, in situations where the amendment is regarding safety issues and there is

an immediate hazard to subjects, the amendment will be submitted as an urgent amendment and can be implemented in the study prior to approval. The Informed Consent and CRFs will be reviewed to ensure these are amended if necessary.

Administrative changes that do not affect the subject benefit/risk ratio (e.g., editorial changes for clarity) may be made without any further approvals.

16.5 Protocol Deviations/Violations and Medical Emergencies

A protocol deviation or violation is a failure to comply with the requirements of the clinical study as specified in the protocol. Examples of protocol deviations include late visits, missed visits, required follow-up testing not completed. An example of a protocol violation includes enrollment of a study subject who fails to meet inclusion/exclusion criteria as specified in the protocol. Each investigator shall conduct this clinical study in accordance with the study protocol and any conditions required by the reviewing IRB.

Deviations/violations from clinical protocol requirements will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective actions put into place. The Sponsor accepts the right of the Investigator to deviate from the protocol in an emergency when necessary to safeguard the life or the physical well-being of a study subject. Such deviations must be reported within 5 working days of implementation to the IRB and Sponsor. The Investigator must give notice of any emergency deviations and justification for the deviation to MC10, Inc. and the IRB as quickly as possible after the episode, in any event no later than 24 hours after the emergency.

Each study site should maintain a list of protocol deviations that can be reviewed by the Sponsor. Subject numbers should be indicated for each protocol deviation on the lists.

16.6 Pre-Study Documentation Requirements

Prior to shipment or receipt of investigational product, the following documents must be provided to the Sponsor:

- Signed protocol/protocol amendments
- Signed and dated Investigator Agreement(s)
- A copy of the written IRB approval of the protocol
- A copy of the written IRB approval of the Informed Consent Form
- Signed and dated Curriculum Vitae of the Investigator(s)
- Copy of the Investigator(s)' current medical license(s), or equivalent
- Signed and dated Non-Disclosure Agreement(s), if required
- Signed and dated Certification/Financial Disclosure Form(s)

16.7 Record Retention

The Investigator will maintain all essential trial documents and source documentation that support the data collected on the study subjects in compliance with FDA and ICH/GCP guidelines. Documents must be retained until at least 2 years have elapsed since the date the investigation is completed or terminated or the records are no longer required to support a regulatory submission, whichever date is later. These documents will be retained for a longer period of time by agreement with the Sponsor or in compliance with other regulatory requirements. The investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the investigator withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility. The Sponsor must receive written notification of this custodial change.

16.8 Criteria for Terminating Study

The Sponsor reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators and associated IRB will be notified in writing in the event of termination.

Possible reasons for study termination include:

- The discovery of an unexpected, significant, or unacceptable risk to the subjects enrolled in the study.
- A decision on the part of the Sponsor to suspend or discontinue development of the device.

16.9 Criteria for Suspending/Terminating an Investigational Site

The Sponsor reserves the right to stop the enrollment of subjects at an investigational site at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/terminating a study center include:

- Failure to obtain written Informed Consent.
- Failure to report SAE or UADE to the Sponsor within 24 hours of knowledge.
- Failure to complete data forms prior to the scheduled monitoring visits.
- Loss of (or unaccounted for) investigational product inventory.

16.10 Sponsor Responsibilities

The Sponsor, MC10, Inc., is responsible for selecting qualified investigators and providing them with the information and materials necessary to conduct this trial appropriately, ensuring proper monitoring of the investigation, and that IRB review and approval are obtained, and ensuring that the Investigators and the reviewing IRB are promptly notified of significant new information about this investigation.

Specifically, the Sponsor will be responsible for:

- Securing compliance with the clinical protocol, Investigator Agreement, and federal, state and local regulations;
- Conducting evaluations of all adverse events;
- Controlling the distribution of the device(s) under investigation;
- Maintaining records and reports;
- Analyzing and reporting data;
- Designating appropriately qualified medical personnel to be available to advise on study-related medical questions or problems
- Addressing any device-related inquiries outside the expertise of the site staff.

16.11 Investigator Responsibilities

- Agree to sign and adhere to the Investigator Agreement.
- Obtain approval from the IRB including subsequent protocol amendments and changes to the Informed Consent form and obtaining annual IRB approval and renewal throughout the duration of the study.

- Await IRB approval, as well as, any additional hospital or facility requirements prior to requesting written informed consent from any potential study subject or prior to allowing any subject to participate in the study.
- Complete and provide signed copies of all required investigator documentation such as an Investigator Agreement or Disclosure of Financial Interest.
- Be willing to perform and be capable of performing study procedures as outlined in this protocol.
- Comply with all required elements of this protocol (e.g., perform testing and follow-up as specified, especially during personnel transitions).
- Agree to obtain written Informed Consent before any study specific procedures are performed in accordance with GCP.
- Control Secure storage area for any investigational device(s) stored at their site.
- Be aware of, and comply with, GCP and applicable regulatory requirements.
- Permit monitoring and auditing by the Sponsor, and inspection by the appropriate regulatory authorities.
- Have available an adequate number of qualified staff and adequate facilities to properly conduct the study.
- Ensure that study personnel are adequately informed about the protocol, the investigational device and study-related duties and functions.
- Provide subject support for device-related questions and subsequently contact the sponsor for any inquiries outside their expertise.

17.0 REVISION HISTORY

Date	Description
	Version 00. Initial Release.

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[8]ISO 10993-10:2010 “Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization”, Annex C, Page 45, 2010.

[9]ISO 10993-10:2010 “Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization”, Annex C, Page 45, 2010.

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