Official Title: Feasibility and Acceptability of Oxygen Saturation Monitoring Using Masimo SafetyNet Alert (MSNA) in a Supportive Housing Program

Date of Protocol: November 14, 2023

NCT Number: NCT06217380

Feasibility and Acceptability of Oxygen Saturation Monitoring using Masimo SafetyNet Alert in a Supportive Housing Program
SAFE0004

Clinical Investigation Title:	Feasibility and Acceptability of Oxygen Saturation Monitoring using Masimo SafetyNet Alert in a Supportive Housing Program
Clinical Investigation Number, Version:	CIP-1027 version 1.1
Other Study Identifier:	SAFE0004
Study Device(s):	Masimo SafetyNet Alert
Sponsor:	Masimo Corporation 52 Discovery Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

Investigation Site(s): [redacted]

Address: [redacted]

IRB: Ottawa Health Science Network Research Ethics Board

Address: Civic Campus Box 675
725 Parkdale Avenue
Ottawa, Ontario K1Y 4E9 Canada

Agreement between Investigator and Sponsor Regarding Responsibilities for Good Clinical Practice

Sponsor and Investigator agree to comply with International Conference of Harmonization (ICH) E6 Good Clinical Practice guidance. ICH E6 GCP guidance is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human participants.

It specifies general requirements intended to:

- Protect the rights, safety and well-being of human participants,
- Ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- Assist sponsors, monitors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

The Principal Investigator of the clinical investigation shall:

- Obtain and maintain REB approval of the study.
- Ensure all participants are consented prior to enrollment, per FDA Code of Federal Regulations titled 21 CFR 50.
- Ensure only appropriately trained personnel will be involved in clinical investigation.
- Maintain study records mentioned in the Clinical Investigation Plan.
- Maintain logs for study team delegation, site visit/monitoring, equipment disposition, study team training, participant recruitment and enrollment.
- Evaluate all adverse events and adverse device effects and determining whether the study is safe to continue.
- Allow the sponsor to conduct periodic monitoring of study activities to ensure GCP compliance.
- Not promote device prior to clearance by FDA for commercial distribution, except for academic purposes and scientific presentations.

The Sponsor shall ensure existence and record of all necessary compliance documents and will conduct monitoring visits to ensure appropriate conduct of the study.

The principal investigator's signature on this page constitutes the investigator's affirmation that he or she is qualified to conduct the clinical investigation, agreement to adhere to all stipulations of this clinical investigation plan, the conditions of the Institutional Review Board (IRB) or Research Ethics Committee approval, federal and local regulatory requirements, 21 CFR 812, ISO 14155, and International Conference on Harmonization Good Clinical Practice (ICH GCP) guidance.

Principal Investigator: [redacted]	**Title:** [redacted]	**Signature:**	**Date:**
Sponsor Representative: [redacted]	**Title:** [redacted]	**Signature:**	**Date:**

1. OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION

Clinical investigation title:	Feasibility and Acceptability of Oxygen Saturation Monitoring using Masimo SafetyNet Alert (MSNA) in a Supportive Housing Program
Study objective(s):	The primary objective of this study is to explore the feasibility of implementing the Masimo SafetyNet Alert (MSNA) oxygen saturation monitoring system and the acceptance of MSNA by individuals living in a supportive housing program, who inject opioids.
Investigational device(s):	Masimo SafetyNet Alert (MSNA)
Number of participants:	Up to 15 unique client participants and 5 staff participants
Inclusion criteria:	Client Participants • Participants who are ≥18 years of age • Participants housed within a supportive housing program who intend to inject opioids • Participants who have given verbal informed consent to participate in the study Staff Participants • Participant is research staff and/or Rita Thompson Residence staff • Participant is willing to give implied consent by reading and completing the staff survey
Exclusion criteria:	Client Participants • Participants deemed not suitable for the study at the discretion of the principal investigator, research staff or housing program nurses/staff • Participants with skin abnormalities at the planned application sites that may interfere with sensor application, per directions-for-use (DFU) or trans-illumination of the site, such as psoriasis, eczema, angioma, burns, scar tissue, substantial skin breakdown, nail polish, acrylic nails, infections, or other abnormalities that may interfere with MSNA functioning • Participants with known allergic reactions to foam/rubber products and/or adhesive tape Staff Participants • None
Duration of the clinical investigation:	60 days
Study endpoint(s):	• Evaluation of feasibility of MSNA in a supportive housing program • Evaluation of acceptability of MSNA in a supportive housing program • Evaluation of integration and expansion of MSNA to similar housing environments

2. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

Masimo Corporation is the developer of noninvasive technologies for the measurement and monitoring of physiological variables, such as arterial oxygen saturation (SpO2), total hemoglobin concentration (SpHb), carboxyhemoglobin concentration (SpCO), methemoglobin concentration (SpMet), and other physiological variables to improve patient outcomes and reduce cost of care. Masimo SafetyNet Alert™ (MSNA) is a continuous non-invasive monitoring and alert system designed to help recognize opioid induced respiratory depression (OIRD) while taking opioids. MSNA consists of the Masimo SafetyNet Alert™ Halo software, smartphone application, sensor, chip, home medical hub, and hosted cloud service.

The MSNA System is comprised of:

- MSNA Halo Software – runs continuously to provide real-time assessments of the risk of severe OIRD based on changes or patterns in the patient's biometric data (SpO2, PR, Pi)
- MSNA App (Smartphone Application)
- Home Medical Hub

- MSNA Cloud (Server or Cloud)
- Masimo Radius PPG wearable pulse oximeter sensor
- Masimo Chip

The MSNA system features an escalating alarm notification system providing both audible and visual cues on the home medical hub and smartphone application. The [redacted] MSNA notification thresholds are:

[redacted]

MSNA monitors physiological parameter data [redacted]. One alarm looks for [redacted] and the other utilizes [redacted] software. [redacted]

For the purposes of this study, the Level 3 EMS feature will be disabled as residence staff are available to respond to critical events.

Research personnel and study participants will be provided with the system's Directions for Use, as well as study-specific instructions in REB-approved supplemental materials. Research personnel will be provided with an Investigator's Brochure with detailed information about the MSNA System.

Traceability of devices shall be achieved during and after the clinical investigation by assignment of lot numbers or serial numbers as applicable.

Product Overview

Item	Description
1	Home Medical Hub
2	Smart phone with Masimo SafetyNet Alert App Installed*
3	Masimo Sensor
4	Masimo Chip

* Smart phone not included

Figure 1. Masimo SafetyNet Alert System product overview.

Product Descriptions

Masimo SafetyNet Alert - a system that provides spot-checking and continuous monitoring of physiological data by wireless communication to medical technologies. The system includes the following pieces:

Masimo SafetyNet Alert App - software application installed on a smart phone that provides the graphical user interface to display your data and alarm condition status.

Masimo Sensor™ - wireless, wearable sensor that provides the physiological data.

Masimo Chip™ - attaches to the wireless Masimo Sensor and connects wirelessly to the Home medical hub.

Home Medical Hub - device that communicates monitoring data wirelessly from the medical technologies to the Masimo SafetyNet Alert Cloud.

Masimo SafetyNet Alert Cloud - a server accessed over the internet that gathers and stores measured data communicated wirelessly from the Home Medical Hub.

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

Opioids have increasingly been implicated etiologically for drug overdose deaths over the last two decades in both USA and Canada. From 1999 to 2013 the rate of drug poisoning deaths involving opioid analgesics nearly quadrupled in the United States.[1] In 2018 among 67,367 drug overdose deaths, 46,802 (69.5%) involved opioids in the United States.[2] This was followed by a significant increase through 2020 to 68,630 overdose deaths.[3] The rate of drug overdose deaths involving synthetic opioids other than methadone (drugs such as fentanyl, fentanyl analogs, and tramadol) continued to increase from 9.0 per 100,000 in 2017 to 9.9 in 2018.[2] Across Canada, over 16,364 opioid-related deaths occurred between January 2016 and March 2020, including 1,018

deaths between January and March 2020, of which 96% were accidental.[4] Prior to the declaration of the COVID-19 pandemic in March 2020, the United States and Canada were in the midst of a drug overdose crisis[5], which has worsened since the onset of COVID-19.[6]

People experiencing homelessness have high rates of substance use, and homelessness may be a critical health disparity factor in the opioid overdose epidemic.[8] The goal of the John Howard Society of Ottawa's Enhanced Supportive Housing programs like the Rita Thompson Residence are to reduce the number of individuals using homeless shelters or living on the street. The program provides semi-independent accommodation and on-site support services. Although these programs address the issue of homelessness, opioid users are still at risk when using alone in their rooms. About 50% of opioid-related deaths occur when a person uses an opioid alone.[10] A recent study conducted in British Columbia, which has the highest toxic drug overdose death rate in Canada, indicated that 75.8% (n = 314) of the study sample reported using drugs alone within the last week at the time of the interview, and 73.2% (n = 230) used opioids.[8]

These statistics highlight the burden of the opioid epidemic that the United States & Canada are experiencing and support the need for innovative medical technologies that may prevent opioid overdose and to provide medical therapies to mitigate the risk of death.[7]

The intent of this study is to prospectively determine both the feasibility of implementing an oxygen saturation monitoring system (MSNA system) in a supportive housing program and the acceptance of the MSNA system by individuals who inject opioids. We will assess the willingness of both residents and housing staff to use this system in this environment, as well as factors to consider for successful implementation of the MSNA system in similar housing environments.

4. BENEFITS AND RISKS OF THE INVESTIGATIONAL DEVICE, CLINICAL PROCEDURE, AND CLINICAL INVESTIGATION

4.1. **Benefits:** Study participants may benefit from the continuous monitoring of their oxygen saturation with MSNA and increased awareness of oxygen desaturations through multiple notification methods managed through an alarm escalation process. MSNA provides capacity for the participant to establish a personalized response network.

4.2. **Radius PPG™ wireless SpO2 sensor (MSNA Sensor) risks:** refer to *Investigator Brochure* and *Directions for Use (DFU)* for full instructions and description of warnings and cautions.

4.2.1. The Radius PPG sensor contains small parts. Small items may become choking hazards. Do not leave the sensor components unattended around children.

4.2.2. The Radius PPG includes a sensor attachment strap. The sensor attachment strap site must be checked frequently to ensure adequate securement, circulation, and skin integrity.

4.2.3. Sensors applied too tightly or that become tight due to edema will cause inaccurate readings and can cause pressure necrosis.

4.2.4. Skin erosion and pressure necrosis may occur in patients with poor perfusion (e.g., peripheral vascular disease) if the sensor is not frequently moved. Caution should be exercised with such patients.

4.2.5. As with all optical sensors, the Radius PPG sensor has the risk of thermal burn. The design includes safeguards, and this risk demonstrably low. All patient-contact materials, including the adhesive used in the design of the Radius PPG sensor, have been subjected to biocompatibility tests per ISO 10993-1 and results demonstrate that the materials are non-toxic, non-irritating, and non-sensitizing. The sensors have been subjected to performance, mechanical, and electrical testing and results demonstrate that the sensors meet the requirements for safety and effectiveness for the intended use of the product.

4.3. **Masimo SafetyNet Alert risks:** refer to *Investigator Brochure* and User's Manual for full instructions and description of warnings and cautions.

4.3.1. There may be electrical, mechanical, or thermal hazards that may lead to patient injury and discomfort. This risk has been mitigated through electrical safety testing in accordance with IEC 60601-1.

4.3.2. There may be a potential for frequent non-actionable alarms to affect the participant's injection through frequent unnecessary interventions. This risk has been mitigated by incorporation of Masimo SET pulse oximeter technology that has been tested under no motion and motion conditions in controlled desaturation studies in accordance with ISO 80601-2-61. Masimo SET pulse oximeters have completed bench testing under low perfusion conditions. MSNA has completed testing to support the wireless communication of the wearable sensor to the home medical hub. MSNA has been designed to feature a notification escalation policy with thresholds to reduce non-actionable alarms.

4.3.3. The research staff and/or participant may fail to properly setup and use the device. This risk has been mitigated by the design of the device that considers the use by lay operators (i.e., non-healthcare professionals). The system has undergone human factors and usability testing to support the safe and effective use by lay operators.

4.3.4. There may be a potential interruption or interference in the communication between the system's components. This risk has been mitigated by specific testing to support the co-existence of communication between components. Electromagnetic compatibility testing to support the system's use around other radio containing devices has been completed.

4.3.5. There may be potential vulnerability to cyberattack that may affect the monitoring or reliable security of the participant's personal information. This risk has been mitigated by the completion of cybersecurity risk analysis and testing to support the incorporation of cybersecurity risk controls.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

The primary objectives of this study are to explore the feasibility of implementation and acceptance of the MSNA system by individuals living in a supportive housing program who injecting opioids.

6. DESIGN OF THE CLINICAL INVESTIGATION

6.1. General

This study is a prospective, single center, nonrandomized, single-arm study. Given the goals of this study, a control group is not necessary. The study endpoints are designed to evaluate the feasibility of implementing an oxygen saturation monitoring system and acceptance of MSNA by individuals living in a supportive housing program who inject opioids.

The study endpoints are:

- Evaluation of Feasibility of MSNA in a supportive housing program
- Evaluation of Acceptability of MSNA in a supportive housing program
- Evaluation of Integration and Expansion of MSNA to Similar Housing Environments

Given the primary goals of exploring feasibility and acceptability, outcome data will utilize descriptive statistics (e.g., summarizing the recruitment rate, proportion of incomplete studies and lost components). Assessments and qualitative feedback will be examined to determine the acceptability of the system within the supportive housing program. Sample feasibility and acceptability questions to be answered from this study are listed below.

[redacted]

[redacted]

6.2. **Investigational device(s) and comparator(s)**

No comparator will be used in this study. All participants will be connected to the MSNA system [redacted]. Data will be collected [redacted]. Research staff will record if any alerts were received to the designated emergency contact number and if any interventions were required. Participants and research staff will record their user-experience feedback for the MSNA system on the CRF.

6.3. **Participants**

6.3.1. Inclusion Criteria

Client Participants

- Participants who are ≥18 years of age
- Participants housed within a supportive housing program who intend to inject opioids
- Participants who have given verbal informed consent to participate in the study

Staff Participants

- Participant is research staff and/or Rita Thompson Residence staff
- Participant is willing to give implied consent by reading and completing the staff survey

6.3.2. Exclusion Criteria

Client Participants

- Participants deemed not suitable for the study at the discretion of the principal investigator, research staff or housing program nurses/staff
- Participants with skin abnormalities at the planned application sites that may interfere with sensor application, per directions-for-use (DFU) or trans-illumination of the site, such as psoriasis, eczema, angioma, burns, scar tissue, substantial skin breakdown, nail polish, acrylic nails, infections or other abnormalities that may interfere with MSNA functioning
- Participants with known allergic reactions to foam/rubber products and adhesive tape

Staff Participants

- None

6.3.3. Study Timelines

[redacted] Each participation will employ [redacted] data acquisition [redacted]. Study will be conducted only when trained research staff is present at the residence. Up to 15 unique participants may be enrolled. We anticipate that this study will require up to 30 days for completion of data collection for n=15 participants.

6.3.4. Client participants will be classified according to the following status:

- Enrolled – all participants who went through the informed consent process and signed the informed consent form.
- Completed – participants who inject while connected to the MSN Alert system at any time during the study period.

- Incomplete - participants who do not inject while connected to the MSN Alert system at any time during the study period.
- Withdrawn – participants who do not complete study either because they voluntarily chose not to participate further in the study and withdrew their consent, or they are discontinued from the study per research staff discretion.

6.3.5. Staff participants will be classified according to the following status:

- Completed – staff participants that provide implied consent and complete the staff survey
- Withdrawn – staff participants who do not complete the survey because they voluntarily chose not to participate further.

6.4. **Procedures**

6.4.1. Standard procedures used at the residence to provide care for their residents that use illegal substances shall be prioritized over any of this research study's procedures.

6.4.2. Orientation- All residents of the facility will be provided with notice that this study is being conducted in the facility and any interested residents will be evaluated for eligibility. A study overview will also be provided to them.

6.4.3. Informed Consent-Trained and delegated research staff will obtain verbal informed consent prior to each participant's inclusion into the study. The consent will be valid for the duration of study or whenever consent is withdrawn if prior.

6.4.4. Eligibility Verification- Investigator and/or research staff delegated for this task shall verify eligibility criteria for the participant on the case report form (CRF). If the participant does not meet all eligibility criteria and they have already been enrolled into the study, they will be notified and removed from the study.

6.4.5. Day 0 - Device Training-

6.4.5.1. Trained research staff will train participants regarding MSNA functions including the alert notification levels. In the MSNA app, the participant or research study staff will enter the name and phone number of the trained research staff to be designated as an emergency contact in case of MSNA Level 2 and 3 alerts.

6.4.5.2. The app will ask for the participant's name, however, the participant's ID number will be entered instead for anonymity purposes. The app will also ask for a phone number, and an email address to enable full MSNA functionality.

6.4.5.3. Research staff will make sure that the participant demonstrates how to properly place the sensor(s) used to collect data and answer any questions the participant may have regarding the system.

6.4.5.4. Research staff will inform the participant that the home medical hub shall remain in the participant's room and should always be plugged in.

6.4.5.5. Research staff will inform the participant that the phone with the MSNA App will remain with the participant during the data collection period (~30 minutes) and MUST be returned to study staff thereafter. The smart device application can display the real-time oxygen saturation and pulse rate readings.

6.4.5.6. Research staff will remind participants to call the front desk [redacted], in their apartment, as per the Rita Thompson Residence standard procedure.

6.4.6. Data Collection Day 1 (Day 0 and Day 1 may be the same day)

6.4.6.1. Research staff will collect and record on the CRF the participant's demographic information, including but not limited to; age, self-identified; gender, race & ethnicity, Massey Scale (skin color) value.

[redacted]

6.4.6.4. Participant shall place the wireless sensor on an appropriate finger and ensure the sensor is connected to the MSNA system. Research staff will first educate participant how to do this, then supervise sensor placement by participant and aid as needed. If assistance is required, research staff shall note on CRF. Refer to Figure 2 for set up of MSNA for data collection.

[redacted]

6.4.6.7. The MSNA system will alarm if any notification level alerts are triggered. Research staff will record on the CRF alarm notification events received on the emergency contact phone.

6.4.6.8. The sensor should stay on the participant [redacted] but may be removed at any time by the participant or by research staff.

6.4.6.9. Research staff will record their observations and/or clinical events that occur [redacted]

6.4.6.10. If an intervention is required, research staff shall record who or what initiated the response on the CRF (i.e., participant, peer, MSNA notification, residence or research staff, etc.)

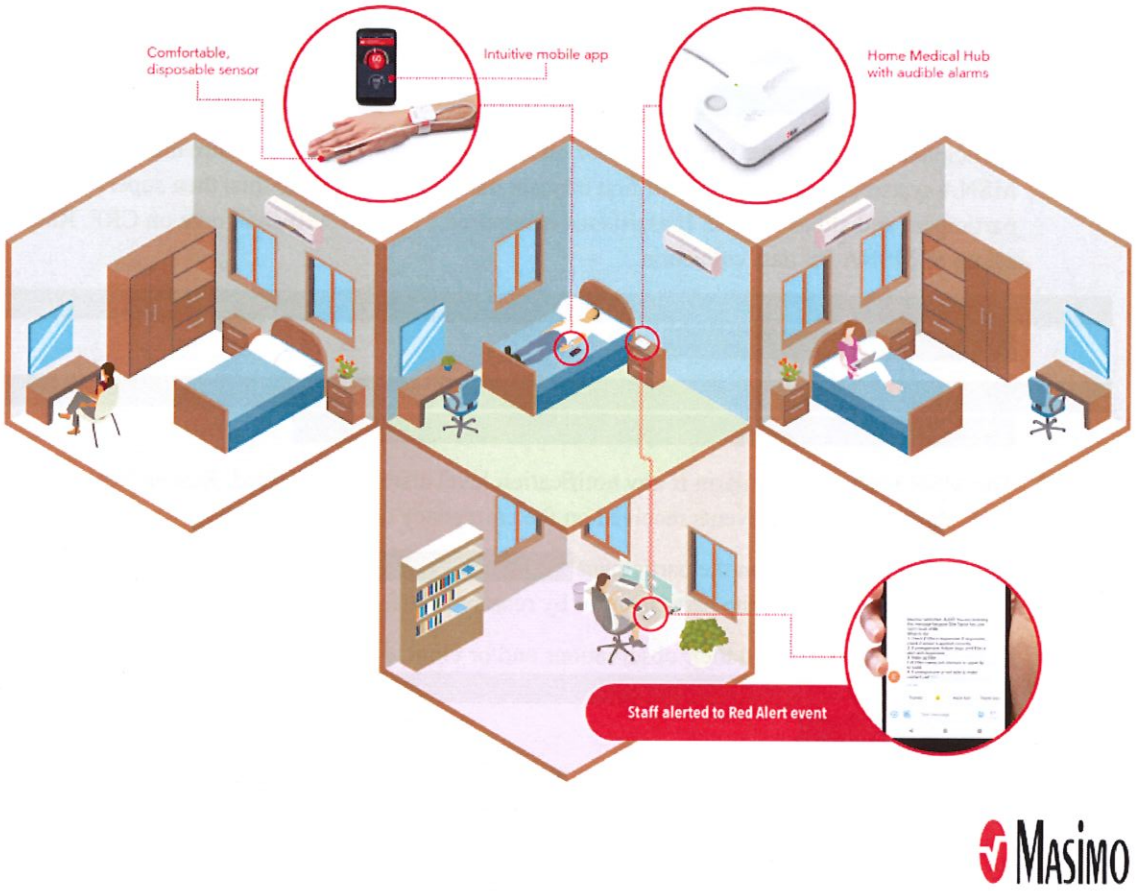

Figure 2. Sample set-up of Masimo SafetyNet Alert at the Rita Thompson Residence for the SAFE0004 study.

6.4.7. Data Collection Day n

6.4.7.1. Research staff shall verify that participant has been previously consented.

6.4.7.2. Research staff or participant shall sign into participant's MSNA App account with their email and password.

6.4.7.3. Research staff shall [redacted] repeat steps 6.4.5.2-6.4.5.10 inclusive.

6.4.8. Staff Participant Survey

Research staff and/or Rita Thompson staff may also complete a survey at the end of the study if they agree to do so. By completing the survey, the consent to participate is implied.

6.4.9. Procedure Evaluation

Throughout this study, procedures may be refined to enable adaptation to site and participant aptitude and attitudes towards the device to enable enhanced understanding of eventual procedural workflows for implementation and use of the device in supportive housing facilities or other similar care areas for persons who use opioid drugs. Research personnel will maintain a journal to record observed participant behaviors, feedback on system implementation and perspectives on device use and value.

6.4.10. Study Completion

Informed consent will be valid for the duration of the study. Participants may choose to discontinue participation in the study at any time. The participant's data collection is considered complete if they inject while connected to the MSNA system at any time during the study period.

6.5. Monitoring plan

As the sponsor of this clinical investigation, Masimo Corporation is required by 21 CFR, Part 812, of the Food and Drug Administration regulations to monitor and oversee the progress of the investigation. The monitor(s) assigned by Masimo Corporation to this task will be trained on departmental SOPs on conduct and monitoring of sponsored studies.

In accordance with good clinical practices guidelines, there will be at least three scheduled monitoring visits to ensure overall regulatory compliance of the study:

- An initiation visit prior to any participant enrollment to confirm site readiness, and to document training on the study protocol and procedures, and use of equipment.
- At least one periodic monitoring visit during initial enrollment, and after approximately every 2 weeks, depending on pace of data collection and any COVID outbreaks, until completion of the study.
- A final close out visit after the last participant has finished the study.
- NOTE DURING COVID-19 PANDEMIC: Monitoring activities may be modified or postponed until such a time that restrictions prohibiting travel and site access are lifted.

Depending on the quality of the data and/or changes to factors affecting patient safety, additional monitoring visits may be necessary at the sponsor's discretion.

The Investigator shall provide the monitor access to all necessary records to ensure the integrity of the data (21 CFR 812). The monitor will verify source documents and records to entries in the CRFs and other GCP-related documents (REB approvals, REB correspondences, and ICFs) if participant confidentiality is maintained, in agreement with local privacy regulations.

It will be the monitor's responsibility to inspect the CRFs at regular intervals throughout the study, to verify the adherence to the CIP and the completeness, consistency and accuracy of the data being entered. During each visit, the monitor will verify presence of informed consent, adherence to the inclusion/exclusion criteria, documentation of SAEs/SADEs and protocol deviations/violations, and check CRF against site records.

After each visit, the monitor will provide a monitoring follow-up letter to the investigator. The follow-up will detail findings and open action items observed during the visit. It is the responsibility of the Principal Investigator and Study Coordinator(s) to respond to the findings of the monitoring letter and complete any open action items as soon as possible. Any open action items not completed within the time allowed may be sufficient grounds for study site suspension or termination; it will be up to the sponsor to determine whether any incomplete action items are sufficient grounds for suspension or termination.

7. STATISTICAL DESIGN AND ANALYSIS

Data collection will continue until enough cases have been obtained with analyzable data (e.g., no data dropouts). This is a feasibility study with no requirements for sample size calculations or statistical considerations.

8. DATA MANAGEMENT

8.1. Data Management and Confidentiality

All documents associated with this protocol will be securely stored in a physical location or on password-protected computers. The confidentiality and retention of these documents will be protected to the extent provided and required by the law. All data will be de-identified before any statistical analysis. Only de-identified data will be shared with Masimo for research purposes

stated in this protocol. Data collected by data capture software and data entered in case report form will be shared with Masimo via a secure, password-protected server that only research staff, and Masimo study team members will have access to. Data will be retained for a minimum to 15 years following completion of the final analysis.

The app will ask for the participant's name, phone number, and an email address to enable full MSNA functionality. However, in lieu of the participant's name, a non-identifying participant ID number will instead be entered into the app. All associated study data for the participant reported as part of this study will only be associated to the anonymized participant ID. Protected health information (PHI) will be stored in the MSNA cloud service but will not be collected or provided to the sponsor as part of study data. The PHI will be participant to Masimo's corporate Privacy Notice and the MSN app's Terms and Conditions.

8.2. Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents and data records include hospital records, clinical and office charts, laboratory notes, memoranda, recorded data from automated instruments, and copies or transcriptions certified after verification as being accurate and complete.

8.3. Case Report Forms

The site shall capture study data in case report forms (CRFs) for each participant enrolled, to be provided to the sponsor. CRFs may be in paper or electronic format through electronic data capture (EDC) software. Masimo shall ensure that systems used for electronic CRFs are compliant with the requirements of 21 CFR Part 11 and ISO / IEC 27001 Certification. The CRFs will be completed and signed by the principal investigator or delegate. This also applies to those participants who fail to complete the study. If a participant withdraws from the study, the reason must be noted on the CRF. Case report forms are to be completed on an ongoing basis. CRF entries and corrections will only be performed by study site staff, authorized by the investigator. For paper CRFs, entries and corrections to the CRF will be made following Good Documentation Practices.

The CRF may include the following information, including but not limited to: inclusion / exclusion criteria, whether participant consent was obtained before start of study, demographic information, device readings, and if occurrence of any adverse event, protocol deviation, and device deficiencies, etc. The CRFs will be signed by the PI or delegate to attest that the data are complete and accurate.

CRF entries will be checked by the study monitor and any errors or inconsistencies will be queried to the site on an ongoing basis. Any changes made within an electronic CRF will be tracked by audit trail. Any changes on a paper CRF will be made directly on the CRF and will be initialed and dated by the person making the change. Query resolution will be assessed and confirmed by study monitor during site visit.

8.4. Data Transfer and Storage

8.4.1. Original paper CRFs will be stored in a secure location at the site. Copy of the original paper CRFs may be scanned and sent to sponsor. If using electronic CRFs, the site staff will be assigned unique usernames and passwords for data security. Final copies of the electronic CRFs in EDC are stored on a secure server.

8.4.2. Only authorized sponsor personnel will have access to study data and will move it to a secure and backed-up drive at Masimo.

8.4.3. CRFs will be checked for completeness and if there are inconsistent or missing data points, queries will be generated. If delegated study staff are to correct the paper CRF, they shall follow GDP practices to strike through old entry, add in new entry, and initial and date it, and provide the corrected information to sponsor. Corrections made to electronic CRFs will be tracked by audit trail and require PI or delegate sign-off.

8.5. Record Retention

Study data will be retained for the necessary period as required by the institution's regulations. Study records shall be retained for a minimum of 15 years after study closure. The Institution's own retention policies and regulations may apply in addition to the minimal requirement.

9. AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

Any changes made to the clinical investigational plan/study protocol will be documented by way of an amendment. Before submitting a protocol amendment to the REB, the protocol amendment must be agreed upon and signed by both the principal investigator and the sponsor. The protocol amendment will be submitted to the REB for approval. At a minimum, a redline version and a clean version of the new protocol amendment will be kept on file by the PI and the sponsor. Protocol amendments will need to be version controlled. Both PI and sponsor will retain the REB approval letter as confirmation that the protocol amendment was approved.

10. DEVIATIONS FROM CLINICAL INVESTIGATION PLAN

Deviations from the protocol must receive both sponsor and the investigator's REB approval before they are initiated, with the exception that under emergency circumstances, deviations from the *Clinical Investigation Plan* to protect the rights, safety and well-being of human participants may proceed without prior approval of the sponsor or the IRB/ethics committee. Any protocol deviations initiated without sponsor and the investigator's IRB/ethics committee approval that may affect the scientific soundness of the study, or affect the rights, safety, or welfare of study participants, must be documented, and reported to the sponsor and to the investigator's REB as soon as a possible, but no later than 5 working days after the occurrence of the protocol deviation. In addition to documenting deviations on the CRF, the *Protocol Deviation Form* may also be used. If protocol deviations continue to occur frequently at a study site, a corrective and preventive action (CAPA) may be opened by the sponsor.

Withdrawal of REB approval: An investigator shall report to the sponsor a withdrawal of approval by the investigator's reviewing REB as soon as possible, but no later than 5 working days of the REB notification of withdrawal of approval.

11. DEVICE ACCOUNTABILITY

11.1. Receipt of Study Device

Upon receipt of the of the study device supplies, an inventory must be performed, and the device accountability log filled out and signed by the person accepting the shipment. It is important that the designated study staff counts and verifies that the shipment contains all the items noted in the shipment inventory. Any damaged or unusable study devices in each shipment will be documented in the study files. The investigator must notify the study sponsor of any damaged or unusable study devices that were supplied to the investigator's site.

11.2. Use of Study Device

Use of device will be documented on case report forms for each participant. Any unused devices must be returned to the sponsor at the end of the study or before product expiration date.

11.3. Return or Destruction of Study Device

At the completion of the study, there will be a final reconciliation of study devices shipped, devices used, and devices remaining. This reconciliation will be logged on the device accountability log. Any discrepancies noted will be investigated, resolved, and documented prior to return or destruction of unused study devices. Devices destroyed on site will only be upon written instruction from the sponsor and will be documented in the study files. When a Masimo device deficiency is observed, every effort should be made to return the device and its packaging to the sponsor in a timely manner.

12. STATEMENTS OF COMPLIANCE

This document is a clinical investigational plan for a human research study sponsored by Masimo Corporation. The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. By participating in the

study, the Investigator agrees to adhere to all stipulations of this protocol, the conditions of the Institutional Review Board (IRB) or Research Ethics Committee approval, federal and local regulatory requirements, 21 CFR 812, ISO-14155, and the International Conference on Harmonization Good Clinical Practice (ICH GCP) guidance.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the REB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the REB before the changes are implemented to the study.

13. INFORMED CONSENT PROCESS

The Investigator and/or staff delegated for this task are responsible for conducting the informed consent process and for obtaining verbal informed consent prior to each participant's inclusion into the study. Participants must provide informed consent prior to being enrolled in the study, in accordance with applicable federal, state and/or provincial regulations.

Subjects in this study will be using substances and participating in activities considered illegal in the United States and Canada. In careful consideration of the study subject's privacy and potential desire for anonymity, a verbal consent process will be used in this study, as approved by the REB. The use of verbal consents is permitted by FDA 21 CFR 56.109(c) and Article 3.12 of Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2018) for studies involving no more than minimal risk. Subject's full names will not be collected in any study documentation.

13.1. Following identification of a potential eligible participant as defined by the inclusion and exclusion criteria, the participant will be approached by the study staff. The study research staff will explain the purpose and procedures of the study with respect to the potential risks, benefits, and clarification of participant's rights & privacy and allow ample amount of time for participating in the described study. The research team will emphasize that participation is voluntary, and declining participation will not affect any services received.

13.2. If the subject expresses interest in participating in the study, verbal consent, as approved by the REB, will be sought from the subject. When seeking verbal consent the study staff will provide information about the study, and the subject will be asked to verbally provide their consent. The subject shall be given adequate time and opportunity to assimilate the information provided, pose any questions they may have, and discuss and consider whether they will participate. Once all questions have been answered and the verbal consent is given, the subject will be enrolled in the study. If the subject refuses to participate, they will not be enrolled in the study. The subject will be assigned a non-identifying subject number for the data collected in this study. The person obtaining consent shall document the verbal consent in the study records.

13.3. The participant shall be provided with a copy of the informed consent document.

13.4. The participant may decline to participate in this study at any time from time of consent.

13.5. The Investigator is also responsible for ensuring any new information related to the study will be provided to the participant. Participant may need to be re-consented to continue participation as required by REB.

13.6. The consent will be valid for the duration of study or whenever consent is withdrawn prior to study completion. Each participant may participate up to 10 times, but no more than once per day.

13.7. Participants must meet all the inclusion criteria and none of the exclusion criteria. If the participant provides oral consent and is identified later as failing to meet all eligibility criteria, the participant will be classified as a withdrawn participant. Upon determination that the participant does not meet all eligibility criteria, the reason for the participant's ineligibility will be documented on a Screening and Enrollment Log.

For the study staff's participation in the study to complete the end-of-study questionnaire, an implied consent process will be utilized, as approved by the REB.

14. ADVERSE EVENTS, ADVERSE DEVICE EFFECTS, AND DEVICE DEFICIENCIES

14.1. Definitions

The definitions for adverse event, adverse device effect, serious adverse event, serious health threat, serious adverse device effect, and unanticipated adverse device effect, device deficiencies are provided below (ISO 14155, 21 CFR 812.3(s)).

- adverse event: untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated (ISO 14155)
- adverse device effect: adverse event related to the use of an investigational medical device
- serious adverse event: adverse event that led to any of the following:
    - a) death
    - b) serious deterioration in the health of the participant, users, or other persons as defined by one or more of the following:
        - 1) a life-threatening illness or injury, or
        - 2) a permanent impairment of a body structure or a body function including chronic diseases, or
        - 3) in-patient or prolonged hospitalization, or
        - 4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,
    - c) fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment

  Note: Planned hospitalization for a pre-existing condition, or a procedure required by the *Clinical Investigation Plan*, without serious deterioration in health, is not considered a serious adverse event.
- serious health threat: signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in participants, users or other persons, and that requires prompt remedial action for other participants, users or other persons.

  Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
- serious adverse device effect: adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
- unanticipated serious adverse device effect: serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

  Note: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
- device deficiency: inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

  Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling.

  Note 2: This definition includes device deficiencies related to the investigational medical device or the comparator.

14.2. **List of non-reportable adverse events**

All adverse events that occur while the participant is wearing the sensor will be reported.

14.3. **Adverse Event Reporting**

- All Adverse Events, both Anticipated and Unanticipated, must be recorded in the within the CRF and in the Adverse Event Report Form.
- All Adverse Events must be promptly reported to the Sponsor.
- All Unanticipated Adverse Device Effects will be also reported to both the Sponsor and the REB.
- Both Serious Adverse Events and Unanticipated Adverse Device Effects must be reported to the Sponsor within 48 hours. All other Adverse Events should be reported to the Sponsor within 5 business days.
- All Serious Adverse Events will be also reported to the REB per REB reporting requirements. These reports may include but will not be limited to: date of onset; brief description of the events; their treatment; whether they resulted in death, inpatient hospitalization, severe or permanent disability or were life threatening; their relationship to the study device; and resolution.

Device Related AEs- Sensor may cause slight, temporary redness, which should fade away shortly after sensor removal.

Opioid Use Related AEs- Includes but not limited to sedation, dizziness, nausea, vomiting, constipation, sedation, overdose, or death.

14.4. **Device Deficiencies Reporting**

All Masimo device related deficiencies should be reported to the sponsor and must be recorded in the CRF in a timely manner. These should be reported to the REB as required per local requirements. When a Masimo device deficiency is observed, every effort should be made to return the device and its packaging to the sponsor in a timely manner.

All Masimo device related deficiencies should be reported to the sponsor and must be recorded in the CRF in a timely manner. This excludes computer issues. These should be reported to the IRB/ethics committee as required per local requirements. When a Masimo device deficiency is observed, every effort should be made to return the device and its packaging to the sponsor in a timely manner.

15. VULNERABLE POPULATION

15.1. **Definition**

Vulnerable populations are research participants, such as children, prisoners, pregnant women, handicapped, or mentally disable persons, or economically or educationally disadvantaged persons, who are likely to be vulnerable to coercion and undue influence.

The federal regulations that govern the protection of human participants require additional protection for any vulnerable population.

15.2. **Protection of vulnerable participants**

- Reasonable compensation will be provided for economically disadvantaged participants to eliminate possibility of undue influence due to financial incentive.
- Educationally disadvantaged participants will be provided ample time to ask questions and comprehend information.

- Medical care will be provided to these participants after the clinical investigation has been completed if they are injured as a direct result of participating in this research study. The cost of treatment for any research related injury will be covered by Masimo.

15.3. Responsible Parties

- The REB will review research with vulnerable populations and evaluate consent, level of risk, coercion, and the reason for choosing this particular participant population. The REB will be responsible for determining what practices will include continuing review for compliance while monitoring these studies.
- The Investigator holds the ultimate responsibility for protecting the rights, safety, and welfare of research participants by ensuring that all regulations and proper documentation of consent is handled in a compliant and timely manner.

16. SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

16.1. Suspension or Termination of Study Site

The sponsor can suspend or prematurely terminate the PI's and study site's participation in the study, particularly if sponsor finds serious non-compliance by the PI or site, and if such non-compliance was not resolved in a timely manner. The sponsor will document the decision to suspend or terminate the investigation in writing. A suspended study site cannot enroll new participants.

If the sponsor determines that the study site's compliance to be inadequate at any point during the study, and sponsor move to suspend or terminate the study site, the sponsor will provide notification in writing to the principal investigator and REB as necessary. The study site is eligible for reinstatement upon correction of any findings and any open action items prior to the suspension and provides a written guarantee that the same non-compliance will not reoccur in the future. Site can only resume participant enrollment upon receiving written notification of reinstatement from the sponsor.

If for any GCP and regulatory non-compliance reasons the study site is prematurely terminated by the sponsor, then the study site is not eligible for reinstatement under the same *Clinical Investigational Plan/Study Protocol.*

16.2. Termination of Clinical Investigation/Study due to UADE

The clinical investigation may be terminated if sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to the participants. Termination shall occur not later than 5 working days after the sponsor makes this determination, and not later than 15 working days after the sponsor first received notice of the effect.

The sponsor may resume the terminated clinical investigation with prior REB approval if the device is non-significant risk.

17. PUBLICATION POLICY

In compliance with 42 CFR Part 11, a study that meets the definition of an Applicable Clinical Trial (ACT) and that is initiated after September 27, 2007, must be registered on ClinicalTrials.gov. Results of the clinical investigation will be made publicly available.

This study is a feasibility and acceptability study and does not meet the definition of an ACT.

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19. REVISION HISTORY

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