Official Title: SpO2 Data Collection in Pediatric Patients Using INVSENSOR00061

Date of Protocol: 02May2023

NCT Number: NCT05896267

Clinical Investigation Title: SpO2 Data Collection in Pediatric Patients using INVSENSOR00061

Clinical Investigation Number, Version: CIP-1080A, version 1.0

Other Study Identifier: BAIL0003

Study Device(s): Masimo INVSENSOR00061 – Investigational

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

1. INVESTIGATOR PAGE

Principal Investigator (s): [redacted]

Investigation Site(s): [redacted]

Address: [redacted]

IRB: WCG IRB

Address: 1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374

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. International Conference of Harmonization (ICH) E6 Good Clinical Practice guidance is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.

It specifies general requirements intended to:

- Protect the rights, safety and well-being of human subjects,
- 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 IRB approval of the study.
- Ensure all subjects 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, subject 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 (REC) 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:**

2. OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION

Clinical investigation title:	SpO2 Data Collection in Pediatric Patients using INVSENSOR00061
Study objective(s):	The objective of this clinical study is to collect data to evaluate the form, fit, and function of INVSENSOR00061.
Investigational device(s):	Masimo INVSENSOR00061
Number of subjects:	Approximately 30 subjects.
Inclusion criteria:	• Subject is a full-term newborn (37 weeks) to 18 months of age.
Exclusion criteria:	• Subject has underdeveloped skin. • Subject has a skin condition and/or deformity at the planned application site, which would preclude sensor placement and measurements. • Subject has an absence or deformities of limbs or severe edema, which would interfere with sensor application or prevent the proper fit of the sensors. • Subject is not suitable for the investigation at the discretion of the Investigator.
Duration of the clinical investigation:	The expected duration of study enrollment is 1 to 3 months. The study devices will be worn for approximately 30 minutes by each subject.
Study endpoint(s):	Evaluate the form, fit, and function of the INVSENSOR00061.

3. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

INVSENSOR00061 is designed to provide parents with access to hospital-grade, clinically proven vitals monitoring technologies, such as Masimo SET®, at home. It is a modified version of the FDA-cleared RD SET® neonatal pulse oximeter sensors which measure temperature and SpO2. The technology of the sensor is similar to the FDA-cleared neonatal sensors but differs in form and fit. The INVSENSOR00061 pulse oximeter sensor is inserted into a silicon bootie holder (Figure 1), that can be worn on either foot, which minimizes sensor slip-off that can result in false alarms. INVSENSOR00061 offers continuous monitoring of blood oxygen

level (SpO_2), respiration rate from the pleth (RRp®), pulse rate (PR), and temperature.

A. **B.**

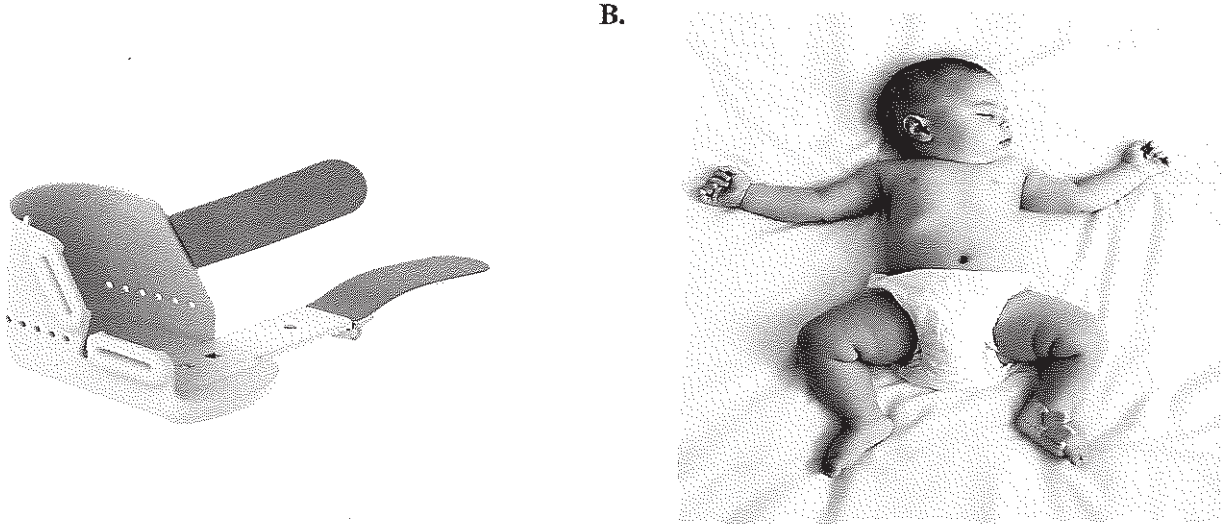

Figure 1. Overview of INVSENSOR00061. **A.** The INVSENSOR00061 used with a bootie that can be worn on either foot, which minimizes sensor slip-off that can result in false alarms. Considering the baby's sensitive skin, the bootie is made from soft silicone material with fabric straps, which is designed for the baby's comfort. **B.** INVSENSOR00061placement on

4. JUSTIFICATION FOR CLINICAL INVESTIGATION DESIGN PLAN

Masimo Corporation develops noninvasive medical technologies such as Masimo Signal Extraction Technology (SET®), which is incorporated in Masimo SET® pulse oximeters and adhesive sensors. Masimo SET® signal processing is designed to overcome limitations of conventional pulse oximetry technologies distinguishing between pulsating blood in arterial and venous blood at the measurement site. Masimo SET® pulse oximeters have been FDA-cleared for the monitoring of the oxygen saturation of blood (SpO_2), pulse rate (PR), and Respiratory Rate from the Pleth (RRp) in motion and non-motion conditions. Masimo SET® pulse oximeters use advanced signal processing algorithms to filter out noise, such as moving venous signals, to help improve the detection of the true arterial oxygen saturation(1).

Blood oxygen saturation level represents the ratio between oxyhemoglobin (oxygenated) and deoxyhemoglobin (non-oxygenated) present in the blood. The pulse oximeter works by measuring frequencies of light, which correspond to the type of hemoglobin present in the blood. By isolating the pulsatile signal, the oxygen saturation of arterial hemoglobin can be estimated.

According to the Centers for Disease Control and Prevention (CDC), in 2020, approximately 3,400 infants died unexpectedly in the United States(3). The three common reasons were Sudden Infant Death Syndrome (SIDS), unknown cause, and accidental suffocation and strangulation in bed, which accounted for 41%, 32%, and 27% of cases, respectively(4). This makes "crib death" (another name used to refer to SIDS) the leading cause of unexpected deaths among infants less than one year old. Masimo INVSENSOR00061 aims to bridge this gap as a continuous monitor of blood oxygen level, respiratory rate, pulse rate, and body temperature. The objective of this study is to evaluate the form, fit, and function of INVSENSOR00061 when used on newborn and infant subjects. Additionally, this data will also be used to provide pilot study estimates of various statistical parameters needed for a future validation study.

To evaluate the form, fit, and function, the study will look to collect data on the application, fit, and ability to obtain the supported parameters on the intended study population. To confirm the acceptability of the form, fit, and function for each subject a standard of care FDA cleared RD SET adhesive sensor will be applied to each subject as a reference for good form, fit, and function. The standard of care sensor is provided as reference in the study because it is possible that a very small population of subjects may have physiologies that may make the supported parameters difficult to obtain.

5. BENEFITS AND RISKS OF THE STUDY DEVICES, CLINICAL PROCEDURE, AND CLINICAL INVESTIGATION

5.1. Anticipated Clinical Benefits

There is no direct benefit to the individual for their participation in this research study. Possible future benefits would be to society as a whole. Development of new technology could enable healthcare workers to recognize and treat potentially life-threatening conditions more appropriately.

5.2. Risks Associated with Participation in the Clinical Investigation

The noninvasive devices used in this study are similar in technology and design to commercially available pulse oximeters and other noninvasive devices and hence have the same risks. Pulse oximeters and other noninvasive devices are commonly used and are considered to be minimal risk.

There is a small risk of damage to the subject's foot from the device, including temporary skin irritation, skin inflammation, itching skin, or discomfort associated with exposure to the sensor, as well as potential temporary mechanical irritation or discomfort. If there are any cuts and/or abrasions near the foot, sensors may not be placed on the particular foot to avoid any discomfort for the subjects.

The sensors have been subjected to performance, mechanical, and electrical testing, skin surface temperature and results demonstrate that the sensors meet the requirements for safety and effectiveness for intended use of the product, refer to investigational brochure for further details.

6. OBJECTIVES OF THE CLINICAL INVESTIGATION

The objective of this study is to evaluate the form, fit, and function of INVSENSOR00061.

7. DESIGN OF THE CLINICAL INVESTIGATION

7.1. General

This is a data collection study using INVSENSOR00061 in the neonatal population. INVSENSOR00061 comes with [redacted] different sizes of booties that can be secured to either foot of the subject. The appropriate size bootie can be determined by following the manufacturer's *Direction for Use (DFU)* referenced in the *Investigator Brochure (IB)*. The confirmation of the form, fit, and function will be assessed based upon ability to obtain readings for the supported parameters after application on the foot. A reference standard of care FDA cleared Masimo RD SET adhesive sensor will also be applied as a reference measurement.

7.2. Investigation Site(s)

This study will be completed [redacted]

7.3. Definition of Completion of the Clinical Investigation

The study will be considered complete after usable data from 30 subjects has been collected and evaluated and a final clinical study report is complete, excluding those who have been withdrawn.

7.4. Study Device(s) and Comparator(s)

Investigational device:

INVSENSOR00061

- A modified version of the FDA-cleared RD SET® neonatal pulse oximeter sensors for measuring SpO_2.
- Contains the same technology as the FDA-cleared neonatal sensors but differs in form and fit. The pulse oximeter sensor is designed to be held using a holder in the form of a bootie that can be worn in either foot, which minimizes sensor slip-off that can result in false alarms.

- Considering the potential for a baby's sensitive skin, the bootie is made from soft silicone material with fabric straps.

Comparators/FDA-cleared References:

- Masimo RD SET® neonatal sensor
- Masimo Radical-7 Pulse CO-Oximeter (or comparable)
- Masimo Root Patient Monitoring System
- FDA-cleared temperature devices (Optional)
- Masimo RAM® sensor (Optional)

Research Equipment

- Laptop with data collection system or smartphone application

7.5. Subjects

7.5.1. Inclusion Criteria

- Subject is a full-term newborn (37 weeks) – up to 18 months of age.

7.5.2. Exclusion Criteria

- Subject has underdeveloped skin.
- Subject has a skin condition and/or deformity at the planned application site, which would preclude sensor placement and measurements.
- Subject has an absence or deformities of limbs or severe edema, which would interfere with sensor application or prevent the proper fit of the sensors.
- Subject is not suitable for the investigation at the discretion of the investigator.

7.5.3. Number of Subjects

Approximately 30 subjects will be enrolled in the study.

7.5.4. Subject Classifications

Subjects will be classified according to the criteria below:

- **Screened** – Subjects who have been approached for participation in the study and have been assessed for study eligibility. after the infant's parent(s), guardian(s), or legally authorized representative (LAR) has reviewed and signed the Informed Consent Form (ICF)
- **Enrolled** – Subjects who have met all the inclusion criteria, do not meet any exclusion criteria, signed the ICF and have been assigned a subject identification number.
- **Screen Failure** – Subjects who do not meet all the screening eligibility criteria (Reason for the subject's ineligibility will be documented on a *Screening and Enrollment Log*).
- **Withdrawn** – Subjects who do not complete the study due to reasons listed below:
  - The infant's parent(s), guardian(s), or legally authorized representative voluntarily withdrew their consent.
  - Subject was discontinued from study at the discretion of the principal investigator (PI).
- **Completed** – Subjects for whom approximately 15 minutes of data has been collected.

7.5.5. Study Duration

Subject participation in the study will be approximately 30 minutes following consent.

7.6. Study Procedures

7.6.1. **Subject Recruitment and Pre-Screening**

A partial waiver of HIPAA authorization will be requested for the pre-screening process of this study. The waiver will allow study staff to access the electronic medical record (EMR) to identify prospective subjects before introducing them to the study and obtaining their informed consent. With this partial waiver, subjects' protected health information (PHI) will remain confidential and will not be disclosed to other individuals. The data collected from this study will not be labeled with any personal identifiers or with a code that will be linked to identifying information.

7.6.2. **Informed Consent Process**

The investigator shall not enroll any subject to participate in the study or consent any subject prior to receiving IRB approval of the informed consent form.

Following identification of a potential eligible subject as defined by the inclusion and exclusion criteria, the subject's parent(s), guardian(s), or legally authorized representative will be approached by the study staff. The study research staff will explain the purpose and procedures of the study, risks and benefits, clarify subject's rights and privacy, and allow ample time for participating in the study. The research team will emphasize that participation is voluntary, has no monetary compensation, and declining the participation will not result in any penalty or loss of benefits that the subject is otherwise entitled.

The investigator(s) and/or staff delegated for informed consent will be responsible for conducting the informed consent process and obtaining the ICF and HIPAA/data authorization form. Informed consent is to be obtained using a form approved by the local IRB and sponsor in accordance with federal and local regulations.

The ICF and the HIPAA/data authorization forms must be signed and dated prior to conducting any study procedures. Informed consent may be obtained either in-person during the subject's pre-operative visit or remotely via phone/videoconference using an electronic form (Adobe sign, DocuSign, REDCap, etc.) as approved by the local IRB and sponsor. If the informed consent is to be conducted remotely, delegated staff will schedule a separate meeting with the subject after the subject is deemed eligible from the screening process. Subjects will be given adequate time to ask questions regarding the study and to discuss with their caregiver, family, and/or friends before making any decisions. Subjects will be informed of the risks and benefits of participating in the study and that their participation is voluntary. After all questions have been resolved, the infant's parent(s), guardian(s), or legally authorized representative may sign the ICF and HIPAA/data authorization form. Both the ICF and HIPAA/data authorization form must be signed in order for the infant to participate in the study. Parent(s), guardian(s), or legally authorized representative may withdraw their infant at any point during the study.

All signed ICF and HIPAA/data authorization forms will be kept with confidential, study-related subject documents in a locked, secure cabinet onsite and accessible only to the research team. A copy of the signed ICF and HIPAA/data authorization form will be provided to the subject.

7.6.3. **Screening**

Information on subject demographics, skin pigmentation using Massey scale, self-identified race/ethnicity, surgical history, and medical history including concurrent medications within the last 90 days will be collected.

Study subjects of differing levels of skin pigmentation will be enrolled in the study. When applicable, subjects with varying demographics e.g., skin pigmentation, gender, etc. may be preferentially recruited to create a more balanced population.

7.6.4. **Data Collection Procedure**

7.6.4.1. A Masimo RD SET® neonatal sensor will be placed on the subject's foot, depending on subject's weight, following manufacturer's DFU and the study's procedure manual. Continuous data from the pulse oximeter will be collected from the Masimo Radical-7 (or comparable) with the Masimo Root Monitoring System.

7.6.4.2. Prior to the placement of INVSENSOR00061, the subject will be observed for crying, restlessness, etc., for approximately [redacted] Observations will be recorded on the case report form (CRF).

7.6.4.3. After approximately [redacted] INVSENSOR00061 will be placed on the opposite foot of the Masimo RD SET® neonatal sensor.

7.6.4.4. An ambient shield(s) will be used to reduce optical interference between sensors.

7.6.4.5. The Masimo RAM® sensor, if used, will be placed on the subject's chest to measure continuous respiration rate.

7.6.4.6. The subject will then be observed for approximately [redacted]

7.6.4.7. After five minutes of observation, INVSENSOR00061 will be paired via Bluetooth connection to Masimo data collection software on a laptop or phone. Upon successful Bluetooth pairing of the investigational device, data collection will be initiated on the data collection software and data will be obtained continuously (SpO_2, PR, RRp, temperature, etc.).

7.6.4.8. Data will be collected for approximately [redacted] using the data collection software.

7.6.4.9. During this timeframe, the subject's temperature, and manual respiratory rate count for [redacted] if required, may be recorded approximately every five minutes.

7.6.4.10. Sensor placement locations, sensor ID/lot number, subject's reaction prior to and after sensors placement, observations during data collection, and other relevant information will be recorded in the CRF.

7.6.4.11. The subject's parent or legal guardian will be asked to complete a survey about their observations and experiences with the device. See Sample survey in Appendix A.

7.7. 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 Standard Operating Procedures (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 subject enrollment to confirm site readiness, and to document training on the study protocol and procedures, and use of equipment.
- At least one monitoring visit during initial enrollment, and/or every 2-4 weeks thereafter until completion of the study.
- A final close out visit after the last subject had finished the study.

The monitor will contact and visit the investigator and will be allowed, on request, to have access to all source documents needed to verify the entries in the CRFs and other GCP-related documents (IRB approvals, IRB correspondences, and ICFs), provided that subject confidentiality is maintained in agreement with HIPAA regulations. The Investigator will provide the monitor access to all necessary records to ensure the integrity of the data (21 CFR 812).

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 on them.

During each visit, the monitor will also verify adherence to the inclusion/exclusion criteria, and documentation of SAEs/SADEs and protocol deviations/violations and check the CRF against source documentation.

After each visit, the monitor will provide a monitoring report to the Investigator within four weeks of visit completion. The monitoring report will detail findings and open action items observed during the visit. It is the responsibility of the PI and study coordinator(s) to respond to the findings of the monitoring report and complete any open action items as soon as possible but no later than 60 days of

[redacted]

receiving the monitoring report. 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.

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

8. STATISTICAL DESIGN AND ANALYSIS

This is a single center prospective study that will use a convenience sampling of 30 subjects. A minimum of 30 subjects are being targeted for this study because it exceeds the 15 typically recommended by the FDA to evaluate the human factors and usability of a device and the number is aligned to the number of subjects calculated by Masimo in which the statistical value of additional subjects diminishes in the Arms error distribution analysis.

8.1. Expected Dropout Rates

Subjects may not complete the study for various reasons, such as clinical screening test failure, at the investigator's or study staff's discretion, or because the subject does not want to continue the study. Due to the short duration and simple, noninvasive procedures of this study, there are limited expected dropouts.

However, the sample size may be increased to account for dropout rates during the study.

9. DATA MANAGEMENT

9.1. 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 the eCRF data capture software will be shared with Masimo via a secure, password-protected server that only study staff and Masimo study team members will have access to. Data will be retained for a minimum of two years following completion of the final analysis.

9.2. 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.

9.3. Case Report Forms

The site shall capture study data in case report forms (CRFs) for each subject 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 PI or delegate. This also applies to those subjects who fail to complete the study.

If a subject withdraws from the study, the reason must be noted on the CRF. The eCRFs are to be completed on an ongoing (weekly) 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 (GDP).

The CRF may include the following information, including but not limited to: inclusion/exclusion criteria, whether subject 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.

9.4. Data Transfer and Storage

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.

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

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, 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.

9.5. Record Retention

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

10. 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 IRB, the protocol amendment must be agreed upon and signed by both the PI and the sponsor. The protocol amendment will be submitted to the IRB 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 IRB approval letter as confirmation that the protocol amendment was approved.

11. DEVIATIONS FROM CLINICAL INVESTIGATION PLAN

Deviations from the protocol must receive both sponsor and the investigator's IRB/ethics committee 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 subjects 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 subjects, must be documented and reported to the sponsor and to the investigator's IRB/ethics committee 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 IRB approval: An investigator shall report to the sponsor a withdrawal of approval by the investigator's reviewing IRB as soon as possible, but no later than five working days of the IRB notification of withdrawal of approval.

12. DEVICE ACCOUNTABILITY

12.1. Receipt of Study Device

Upon receipt 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 a given 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.

12.2. Use of Study Device

Use of device will be documented in a CRF module for each subject. Any unused devices must be returned to the sponsor at the end of the study or before product expiration date.

12.3. 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 onsite 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.

13. 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 IRB or Research Ethics Committee approval, federal and local regulatory requirements, 21 CFR 812, ISO-14155, ICH GCP guidance.

The protocol, ICFs, recruitment materials, and all subject materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study.

14. INFORMED CONSENT PROCESS

See subsection on *Informed Consent Process* under *Study Procedures*.

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

15.1. 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 subjects, 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 subject, 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-subject 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 of subjects, users or other persons, and that requires prompt remedial action for other subjects, 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.

15.2. List of Anticipated Adverse Events

15.2.1. Anticipated Device-Related Adverse Events

The noninvasive device used in this study is similar to commercially available pulse oximeters and hence has minimal risks. Pulse oximeters and other non-invasive devices are commonly used and are considered to be minimal risk.

There is a low risk of temporary skin irritation and/or discomfort where sensors are placed. There is a remote risk of a burn from the sensor. In the case of a sensor burn, there is the potential for permanent skin damage (scar/discoloration).

15.3. 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 IRB.
- 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 five business days.

- All serious adverse events will be also reported to the IRB per IRB 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, subject hospitalization, severe or permanent disability or were life threatening, their relationship to the study device, and resolution.

15.4. 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. 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.

16. VULNERABLE POPULATION

16.1. Definition

Vulnerable population are research subjects, 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. This study is not targeting these populations.

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

16.2. Protection of Vulnerable Subjects

- For children, the Investigator will ensure that parent/legal guardian does not unduly influence subjects to participate (21 CFR Part 50). Parents/legal guardian of the participant will have ample time to ask questions and understand the information being presented.
- As the investigation does not involve monetary compensation for participation, there is no possibility of undue influence due to financial incentive.
- Educationally disadvantaged parent(s) or LAR(s) of subjects will be provided ample time to ask questions and comprehend information.
- Medical care will be provided to these subjects 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.

16.3. Responsible Parties

- The IRB will review research with vulnerable populations and evaluate consent, level of risk, coercion, and the reason for choosing this particular subject population. The IRB 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 subjects by ensuring that all regulations and proper documentation of consent are handled in a compliant and timely manner.

17. SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

17.1. 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 subjects.

If the sponsor determines that the study site's compliance to be inadequate at any point during the study, and the sponsor moves to suspend or terminate the study site, the sponsor will provide notification in writing to the PI and IRB 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 subject 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.*

17.2. Termination of Clinical Investigation/Study due to UADE

The clinical investigation may be terminated if the sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to the subjects. Termination shall occur no later than five 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 IRB approval if the device is non-significant risk.

18. 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 this clinical investigation will be made publicly available on the ClinicalTrials.gov website.

19. BIBLIOGRAPHY

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