Official Title: Form, Fit, and Function of INVSENSOR00061

Date of Protocol: April 03, 2024

NCT Number: NCT05926648

Clinical Investigation Title: Form, Fit, and Function of INVSENSOR00061

Clinical Investigation Number, Version: [redacted]

Other Study Identifier: N/A

Study Device(s): INVSENSOR00061

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

Investigation Site(s): Clinical Laboratory, Masimo Corporation

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Agreement between Investigator and Sponsor Regarding Responsibilities for Good Clinical Practice

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 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:	Form, Fit, and Function of INVSENSOR00061
Study objective(s):	The objective of this study is to evaluate the form, fit, and function of INVSENSOR00061 in generally healthy subjects ages 0-18 months.
Investigational device(s):	Masimo INVSENSOR00061
Number of subjects:	Approximately 25 subjects
Inclusion criteria:	Refer to section 6.3.1.
Exclusion criteria:	Refer to section 6.3.2.
Duration of the clinical investigation:	The expected duration of study enrollment is 1 to 3 months. The expected duration of each subject's participation in the lab will be approximately 120 minutes (2 hours). Subject may participate in home studies with an expected duration of approximately 2 days (48 hours).
Study endpoint(s):	Evaluate the form, fit, and function of INVSENSOR00061

2. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

Masimo Corporation and Cercacor develop noninvasive medical technologies. These devices may have applications in a home setting, the operating room, critical care unit, emergency room, emergency transport vehicles, alternative (home) care, as well as physician's offices.

2.1. FDA Cleared/Consumer Noninvasive Sensors and Devices

Masimo Patient Monitoring Platform (Root® or comparable)

Root is a patient monitoring and connectivity platform that offers rainbow® and Masimo SET® measurements with other parameters in an integrated platform. With docking capabilities for the Radical-7® handheld monitor and Radius-7™ patient-worn monitor and multiple networking/connectivity options, Root integrates multiple streams of data into one display monitor.

Pulse Oximeter Sensors and Cables (Masimo SET®, Masimo rainbow®, or comparable)

Masimo rainbow and SET noninvasive pulse oximeter sensors vary in LEDs and parameters enabled in the sensor. Masimo pulse oximeters may also differ in intended care areas such as spot check or continuous measurements, design of sensor application such as finger clips or adhesive, and patient population such as adults, neonates and pediatrics.

2.2. Investigational Devices

Masimo INVSENSOR00061

INVSENSOR00061 is designed to provide parents with access to hospital-grade, clinically proven vitals monitoring technologies, such as Masimo SET®, at home. INVSENSOR00061 offers continuous monitoring of blood oxygen level (SpO2), pulse rate (PR), [redacted]. INVSENSOR00061 is inserted into a bootie holder so that it can be held in place on the subject's foot. The bootie holder which is made from a soft silicone material with fabric straps, [redacted].

2.3. Site Information

The Masimo Clinical Laboratory facility is designed as a Phase 1 clinical study research center. The laboratory is staffed by physicians, anesthesiologists, certified registered nurse anesthetists, registered nurses, medical assistants, and clinical research staff. All personnel undergo routine required training on GCP and human research subject protections. The laboratory is equipped with standard FDA-approved medical monitoring equipment including ECG monitors, blood pressure monitors, pulse oximeters, standard hematology analyzers, and has emergency crash carts available. Hospitals and urgent care facilities are within three miles of the Masimo Clinical Laboratory.

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

Pulse oximetry is commonly used as a standard of care (SOC) in critically ill patients in intensive care units and used in surgical operations to monitor oxygen saturation (SaO2) levels. The advantage of this noninvasive technology is that it allows for the detection of hypoxia [1].

Oxygen saturation levels represent the ratio between oxyhemoglobin (oxygenated) and deoxyhemoglobin (non-oxygenated) present in the blood [2]. 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.

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 SpO2, PR, and RRp in motion and non-motion conditions. Studies have found fewer false alarms and more accurate true alarm detection. 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 [3].

The objective of this study is to evaluate the form, fit, and function of INVSENSOR00061 when used on newborn and infant subjects. 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 adhesive sensor will be applied to each subject as a reference. 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.

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

4.1. Anticipated Benefits

There would be no medical benefits to the subject. Other possible benefits would be to society as a whole. Development of new technology could enable healthcare workers to more appropriately recognize and treat potentially life-threatening conditions.

4.2. Risks/Discomforts Associated with Participation in the Clinical Investigation

The studies will be conducted per IRB-approved procedures. The study subjects will consist entirely of generally healthy volunteers. The readings obtained during the study will be recorded, but will not be used in patient care, monitoring, or diagnosis.

- **Risks Associated with the Device**

  The noninvasive devices used in this study are similar in technology and design to some 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.

There is a remote, yet possible, risk of a burn from the sensor. In the case of a sensor burn, there is the potential for permanent skin damage (scar/discoloration).

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 subject.

- **Risks Associated with Skin Preparation**

  Subjects may be asked to use an alcohol pad or comparable on the area of sensor application to allow the sensors to adhere to the skin. Risks associated with the skin preparation include rash, flushing or redness of the skin, unusually warm skin, skin inflammation, and/or skin irritation. Each of these discomforts and side effects are temporary and should fade over time.

  If there are any cuts and/or abrasions near the area of sensor application, certain types of skin preparation materials may not be used on the particular location to avoid any discomfort for the subject.

- **Risks from Inflicted Knowledge**

  The risk of inflicted medical knowledge to subjects is negligible since we de-identify all associated information including those relevant to our clinical and engineering parameter studies. The monitoring and test results are not examined for diagnostic purposes and do not reflect an attempt to ascertain any subject's medical condition. The attending physician's role during this study is to ensure the safety of the subject during the study.

  We will reduce the risk of inflicted knowledge by assuring the subject's parent(s) that the device readings are for research use only. In the case that the subject's parent(s) become aware of a condition (hypertension, arrhythmia, etc.) they have during the course of our study, our study staff will recommend that they contact their primary care physician and we will document this recommendation. As part of that process, we will follow up with these individuals prior to enrollment if their condition meets exclusion criteria for a study.

- **Risks from Loss of Confidentiality**

  Masimo upholds the highest standards to protect hard and electronic data, however, a complete promise for confidentiality cannot be guaranteed due to unforeseeable events.

4.3. Emergency Response Plan for Medical Emergencies

A crash cart equipped with medications to provide immediate care during emergencies is on site and full emergency services are within 3 miles.

Study staff will dial 911 for medical emergencies that require emergency medical services (EMS) to be contacted.

4.4. Alternatives

The alternative is to not participate in the study.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

The objective of this study is to evaluate the form, fit, and function of INVSENSOR00061 in generally healthy subjects ages 0-18 months.

6. DESIGN OF THE CLINICAL INVESTIGATION

6.1. General

6.1.1. Clinical Investigation Design

This is a nonrandomized single arm study wherein all subjects are enrolled into the experimental arm and have Masimo INVSENSOR00061 placed on their foot.

6.1.2. Measures Taken to Minimize/Avoid Bias

Subjects are selected from the population surrounding the test site [redacted] Where applicable, subjects with required demographics (skin pigmentation, race/ethnicity, age, gender, etc.) may be preferentially recruited.

6.1.3. Equipment and Materials

Equipment and materials are to be used as required. All lab equipment will be maintained per manufacturer specifications and all study personnel will be trained in the use of relevant equipment.

Safety Equipment (FDA-Cleared)

- Masimo Patient Monitoring Platform (Root® or comparable)
- Masimo Pulse Oximeters (Radical-7®, Rad-97™, Radius-7®, or comparable)
- Pulse Oximeter Sensors and Cables (Masimo SET, Masimo rainbow, or comparable)
- Medical-grade oxygen tank and mask
- Blood pressure monitoring system
- Electrocardiogram (ECG)
- Crash cart

Test Devices (FDA-cleared, consumer products, or investigational)

- Masimo INVSENSOR00061
- FDA-cleared pulse oximeter

[redacted]

Research Equipment

[redacted]

6.1.4. Standard Safety Precautions

Any emergency drug deliveries in the case that a subject loses consciousness or has another emergency arise shall be recorded. This individual will be monitored, and this information will be recorded and submitted to the IRB if necessary, as outlined in section 14.3. The subject will be given the option to follow up with a local urgent care facility.

The subject will be monitored through observation by clinical study staff throughout the study procedure.

An additional pulse oximeter may occasionally be used for the duration of the study to monitor subjects' vital parameters to ensure their safety.

All adverse events will be recorded.

The subject's parent(s) will be informed of the type of procedure that they will be participating in before enrollment in the study.

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

Refer to section 2 for the description of devices that may be used in this investigation.

6.3. Subjects

Potential subjects may be recruited and enrolled according to the criteria below. [redacted]

6.3.1. Inclusion Criteria (Eligible Subjects)

- Subject is a full-term newborn (37 weeks) – up to 18 months of age.
- The parent(s) or guardian(s) of minor subjects are able to read and communicate in English and understand the study and the risks involved.

6.3.2. Exclusion Criteria (Ineligible Subjects) (* = Per study staff discretion)

- 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 has any medical condition which in the judgment of the investigator and/or study staff, renders them ineligible for participation in this study or subject is deemed ineligible by the discretion of the investigator/study staff.

6.3.3. Expected Duration of Each Subject's Participation

The expected duration of each subject's participation in the lab will be approximately 120 minutes.

Subjects may also participate in home studies that may last up to 2 days (48 hours).

6.3.4. Withdrawal of Subjects

Subjects must be withdrawn under the following circumstances:

- The subject's parent withdraws permission.
- Discretion of investigator/study staff.
- Subject safety concerns.

6.3.5. Re-contacting Subjects

If the subject's parent(s) or legal guardian fail to provide proper documentation on their individual permission form for any study, Masimo has the right to re-contact the subject's parent(s) or legal guardian and ask them to return to the clinical lab in order to properly complete the permission form or subject bill of rights. The subject will be compensated for travel.

The subject's parent(s) or legal guardian will also fill out other study documents. These documents aid in the collection of data, tracking subject count, etc. If the subject's parent(s) or legal guardian fails to provide proper documentation on other documents, the subject will not need to return to the laboratory

in order to complete those specific forms. However, Masimo has the right to re-contact the subject's parent(s) or legal guardian and ask them to return to the clinical lab in order to properly complete these documents if seen as necessary by study staff.

The subject's parent(s) or legal guardian will be re-contacted via phone or email and be asked to return as soon as possible.

6.4. Procedures

6.4.1. Recruitment and Pre-Screening

6.4.1.1. Advertisement and Recruitment

Recruitment materials are posted publicly in local newspapers, advertisement websites (e.g., craigslist), schools/universities, social media platforms (e.g., Facebook), bulletins, flyers, handouts, child daycare centers, etc. We will recruit human subjects, which will include members of the general public [redacted].

6.4.1.2. Phone Screening

Once the potential subject's parent(s) or legal guardian see the recruitment material (e.g., advertisement), they can contact us to inquire more details about the study. The recruitment process is managed by the designated person(s) who is trained for phone screening/scheduling.

Virtual or In-person appointments are made once the phone screening process is completed and the person screening the subject determines if they qualify for the study based on inclusion/exclusion criteria.

Information from the screening will be kept in a database located within the firewall-protected Masimo internal network with user level access control enforced domain log in. Additionally, the database is encrypted and password protected. The information is kept to contact the subject's parent(s) for other studies they may qualify for or for instance, to track subjects who call in and provide false information only to qualify.

6.4.2. In-Person Permission and Screening

The subject's parent(s) or legal guardian may be asked to provide a copy of their valid government photo ID and/or Social Security Number (SSN) card to complete a W-9 form. A W-9 form might need to be completed to report earnings to the Internal Revenue Service (IRS).

Foreign persons (a foreign person includes a nonresident alien individual and certain foreign entities that are not U.S. persons) may be asked to provide a copy of U.S. immigration documents/Tax ID Number (TIN) or equivalent, and to complete a W-8BEN form to report earnings to the Internal Revenue Service (IRS).

Copies of these forms of identification may be stored electronically. The confidentiality and retention of these documents will be protected to the extent provided and required by the law.

Copies of the SSN and ID card are kept to verify subjects' identities or for instance, to track subjects who provide false identification.

For all subjects, a parent or legal guardian must be present throughout the duration of the study. The parent or legal guardian must read and sign the parental permission form for their child to participate, using our informed consent process.

The paper parental permission form must be stamped with a current IRB approval. Due to the limitations of the electronic parental permission form, the form may not be stamped with a current IRB approval; however, the IRB will review and approve the electronic document prior to implementation. The electronic parental permission form will contain indicators that show the version of the form. No study-related activities will be conducted until the parental permission form is completed by the subject's parent(s) or legal guardian.

Study documents such as the Confidentiality Agreement and Volunteer Payment Form will be

completed by the subject's parent(s) or legal guardian.

A parent or legal guardian must complete the health assessment on the subject's behalf. Subjects who do not meet the inclusion criteria and/or meet exclusion criteria will not be eligible to participate in the study.

Subject demographic information such as age, sex, skin tone, ethnicity, height, and weight will be collected. These may be recorded for data analysis and/or subject safety monitoring purposes. [redacted]

During the study, subjects may be recorded using photography and/or videography. The recordings may include sound. These recordings may capture identifying features. These recordings may be used in research, product development, product testing, training, and comparison study purposes. In studies with photography and/or videography, the subject's parent(s) or legal guardian will give permission for the recordings and/or observational group prior to the start of any study-related activities.

6.4.3. Virtual Permission and Screening

The parent or legal guardian must read and sign the parental permission form for their child to participate, using our informed consent process.

The parental permission form may be sent out electronically or on paper. The paper parental permission form must be stamped with a current IRB approval. Due to the limitations of the electronic parental permission form, the form may not be stamped with a current IRB approval; however, the IRB will review and approve the electronic document prior to implementation. The electronic parental permission form will contain indicators that show the version of the form. No study-related activities will be conducted until the parental permission form is completed by the subject's parent(s) or legal guardian.

Study documents such as the Confidentiality Agreement and Volunteer Payment Form will be completed by the subject's parent(s) or legal guardian.

Delegated lab personnel will call the parent or legal guardian to complete the health assessment on the subject's behalf. Subjects who do not meet the inclusion criteria and/or meet exclusion criteria will not be eligible to participate in the study.

Subject demographic information such as age, sex, skin tone, ethnicity, height, and weight will be collected over the phone. These may be recorded for data analysis and/or subject safety monitoring purposes. [redacted]

The subject's parent or legal guardian may be asked to provide photos or videos of sensor placement on the subject. In studies with photography and/or videography, the subject's parent(s) or legal guardian will give permission for the recordings and/or observational group prior to the start of any study-related activities.

6.4.4. In-Person Sensor Placement Procedure and Data Collection

Prior to the placement of INVSENSOR00061, the subject may be observed for crying, restlessness, etc. If applicable, the observations will be recorded on the subject's CRF.

The area of sensor application may be prepped using an alcohol pad or comparable. INVSENSOR00061 will be placed on the opposite foot of the FDA-cleared sensor.

An FDA-cleared 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.

[redacted]

[redacted]

INVSENSOR00061 will be paired via Bluetooth connection to data collection software on a laptop or a 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, [redacted]).

Data will be collected for approximately 90 minutes using the data collection software. The subject may be observed for crying, restlessness, etc. If applicable, the observations will be recorded on the subject's CRF.

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

6.4.5. Virtual Sensor Placement Procedure and Data Collection

The subject's parent(s) or legal guardian may be asked to prep the area of sensor application using an alcohol pad or comparable which will be provided. INVSENSOR00061 may be placed on the opposite foot of the FDA-cleared sensor.

An FDA-cleared sensor may be placed on the subject's foot, depending on subject's weight, following manufacturer's DFU. Continuous data from the pulse oximeter will be collected via Bluetooth.

[redacted]

[redacted]

INVSENSOR00061 will be paired via Bluetooth connection to data collection software on a laptop or a 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, [redacted]).

Data may be collected overnight while the subject is asleep for up to two days using the data collection software. The subject may be observed for crying, restlessness, etc. If applicable, the observations will be recorded in the data collection device.

Standard of care and the study sensor placement locations, study sensor ID/lot number, the subject's reaction prior to and after sensors placement, observations during data collection, and other relevant information may be recorded in data collection device.

6.4.6. Ending Procedure

At the conclusion of the procedure, the sensor(s)/device(s) will be removed and returned to Masimo either by mail or in-person drop-off if applicable.

[redacted]

The subject's parent(s) or legal guardian will be paid according to the compensation breakdown on the permission form.

6.5. Monitoring plan

A separate document for the study monitoring plan will be developed and followed to ensure subject safety and GCP compliance.

7. STATISTICAL DESIGN AND ANALYSIS

This is a single center prospective study that will use a convenience sampling of 25 subjects. A minimum of 25 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.

As part of the additional data analysis for this study, the [redacted] accuracy values may be calculated against the respective reference. The purpose of this study is to assess the form, fit, and function, the analysis is not intended for specification validation. The performance specification validation is outside the scope of this convenience sample study.

[redacted]

- Accuracy (root mean square error [A_{RMS}])

[redacted]

$$A_{RMS} = \sqrt{\frac{\sum_{i=1}^{n}(Test - Ref)^2}{n}}$$

7.1. 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.

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 study staff and Masimo study team members will have access to. Data will be retained for a minimum to 2 years following completion of the final analysis.

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: 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 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 principal investigator 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. 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 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.

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 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.

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 IRB, 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 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.

10. 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 5 working days of the IRB 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 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.

11.2. Use of Study Device

Use of device will be documented on case report forms for each subject. 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, 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 Institutional Review Board (IRB) 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 IRB before the changes are implemented to the study.

13. INFORMED CONSENT PROCESS

Subject's parent(s) or legal guardian must read and sign the consent document using the informed consent process as outlined in FRM-3451 Informed Consent Process. No study-related activities will take place prior to informed consent.

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 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-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 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 labelling.

  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, including inter-current illnesses, will be reported and documented as described below.

Refer to section 4.2 for the description of anticipated adverse events.

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 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 5 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, inpatient hospitalization, severe or permanent disability or were life threatening; their relationship to the study device; and resolution.

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. 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 population are research participants, such as children, prisoners, pregnant people, 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 subjects require additional protection for the vulnerable population.

15.2. Protection of vulnerable subjects

- Minors (less than 18 years of age) may participate in this study. Parental permission is required for a minor to participate. The parents or legal guardians are given ample time to ask questions. See section 6.4.2. for a description of permission forms that will be completed by their parents/legal guardians.
- Reasonable compensation will be provided for economically disadvantaged subjects to eliminate possibility of undue influence due to financial incentive.
- Educationally disadvantaged subject's parent(s) or legal guardians 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.

15.3. Responsible Parties

- The EC/IRB will review research with vulnerable populations and evaluate consent, level of risk, coercion, and the reason for choosing this particular subject population. The EC/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 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 subjects.

If the sponsor determine 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 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.

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 subjects. 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 IRB 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 is a data collection protocol and does not meet the definition of an ACT.

18. BIBLIOGRAPHY

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19. REVISION HISTORY

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
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