Official Title: Performance of Masimo INVSENSOR00057 in Detecting Atrial Fibrillation (Afib)

Date of Protocol: 27Jun2022

NCT Number: NCT05472012

Clinical Investigation Title: Performance of Masimo INVSENSOR00057 in Detecting Atrial Fibrillation (Afib)

Clinical Investigation Number, Version: [redacted]

Other Study Identifier: [redacted]

Study Device(s): Masimo INVSENSOR00057 - Investigational

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

Investigation Site(s): [redacted]
Address: [redacted]

IRB: WCG IRB
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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. 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 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:	Performance of Masimo INVSENSOR00057 in Detecting Atrial Fibrillation (Afib)
Study objective(s):	The objective of this study is to gather data to validate the performance of Masimo INVSENSOR00057 in detecting atrial fibrillation.
Investigational device(s):	Masimo INVSENSOR00057
Number of subjects:	Approximately 100 subjects.
Inclusion criteria:	• Subject is 18 years of age or older. • Subject is confirmed to have active atrial fibrillation at the time of enrollment.
Exclusion criteria:	• Subject is confirmed to have concurrent active arrhythmias (e.g., PVCs, bradycardia, etc.) at the time of enrollment. • Subject is allergic to adhesives or ECG gel. • Subject whose skin is not intact in or at the vicinity of the device placement site.
Duration of the clinical investigation:	The expected duration of study enrollment is 1 to 3 months.
Study endpoint(s):	Sensitivity and specificity of Masimo INVSENSOR00057 Afib detection function

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 INVSENSOR00057 is a standalone wearable health monitor that combines the functionality of a pulse oximeter monitor and sensor into a single portable device that fits on a user's wrist. The device allows continuous monitoring of multiple parameters, including oxygen saturation (SpO2), pulse rate (PR), respiration rate (RR), as well as an electrocardiogram (ECG) function that includes atrial fibrillation detection. The device pairs via Bluetooth to a Masimo smartphone application that provides continuous health data to the user.


[redacted]

Figure 1: Masimo INVSENSOR00057

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

There are an estimated 46 million individuals suffering from atrial fibrillation, the most common type of cardiac arrhythmia characterized by high frequency of the atrium. Patients with atrial fibrillation have approximately a 4-fold increased risk of mortality compared to the general population (Lee et al., 2018). In addition to increased risk of death, atrial fibrillation also

increases risk of heart failure and stroke. The imminent risks of stroke can be mitigated with prompt administration of anticoagulants (Piazza et al., 2018).

Certain populations are more vulnerable to atrial fibrillation than others; studies have indicated that risk factors for increased risk include older age, sedentary lifestyle, obesity, smoking, diabetes mellitus, hypertension, and obstructive sleep apnea (Staerk et al., 2018). Detecting atrial fibrillation in its early stages can significantly reduce the high disability and mortality rate. A study reviewing the prevalence of atrial fibrillation in 2009 estimated that 700,000 cases were undetected, comprising 13.1% of all cases; half of these projected cases of undiagnosed atrial fibrillation were at increased susceptibility to stroke (Turakhia et. al, 2018).

The intent of this study is to validate the performance of Masimo INVSENSOR00057 in detecting atrial fibrillation. The standard for diagnosis of atrial fibrillation is use of an electrocardiogram (ECG); advancement of this technology, especially via wearable technology, for early detection can improve the prognosis for patients and enable them to seek medical care before the arrhythmia progresses into more adverse complications.

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

4.1. Anticipated Benefits

There will be no direct benefits to the enrolled subjects. Other possible benefits would be to society as a whole. Development of new ECG technologies could enable users to monitor and identify potentially life-threatening conditions more appropriately.

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

The following risks/discomforts associated with study procedures are anticipated adverse events. All adverse events will be documented and reported following procedures outlined in this document.

The noninvasive device used in this study are similar in technology and design to commercially available wearable noninvasive devices. There is a risk of discomfort to the subject's wrist from the device, which may include temporary skin irritation, skin inflammation, itching skin, or discomfort associated with exposure to the device, as well as potential temporary mechanical irritation or discomfort. If there are any cuts and/or abrasions near the application site, the subject will be excluded from the study to avoid any discomfort.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

The objective of this study is to gather data to validate the performance of Masimo INVSENSOR00057 in detecting atrial fibrillation. The noninvasive ECG measurements will be compared to results obtained from an FDA-cleared ECG monitor.

6. DESIGN OF THE CLINICAL INVESTIGATION

6.1. General

This is a prospective, nonrandomized, single arm study. The study endpoints are designed to validate the performance of Masimo INVSENSOR00057 in detecting Afib. The validation of the Afib detection function in the investigational device may be determined using data collected from this study, in addition to data from other Masimo sponsored studies.

The primary endpoint of this study will be the analysis of sensitivity and specificity of Masimo INVSENSOR00057 Afib detection function when compared to data collected using an FDA-cleared ECG monitor.

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

The study will collect data to validate the performance of the Afib detection function of INVSENSOR00057 as compared to a FDA-cleared ECG monitor.

6.3. Subjects

Inclusion Criteria

- Subject is 18 years of age or older.
- Subject is confirmed to have active atrial fibrillation at the time of enrollment.

Exclusion Criteria

- Subject is confirmed to have concurrent active arrhythmias (e.g., PVCs, bradycardia, etc.) at the time of enrollment.
- Subject is allergic to adhesives or ECG gel.
- Subject whose skin is not intact in or at the vicinity of the device placement site.

6.4. Procedures

6.4.1. Recruitment and Pre-Screening

Subjects will be recruited from local clinics or cardiology offices. Subjects who present with active atrial fibrillation during their regular doctor visit will be recruited for the study.

6.4.2. Consenting and Screening

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 or exclusion criteria, the subject will be approached by the study staff. Study staff will explain the purpose and procedures of the study with respect to potential risks and benefits, and clarification of the subject's rights and privacy information. Ample time will be given to review the consent form. The research team will emphasize that participation is voluntary and declining participation in the study will not result in any penalty or loss of benefits that the subject is otherwise entitled.

Once the subject's questions have been answered and the consent documents are signed and dated, the Principal Investigator or delegate will also sign the informed consent documents, approving that the subject will be enrolled in the study. The investigator shall retain the original copy of the signed informed consent documents in each subject's records and provide a copy to the subject. No study related activities will be conducted until the consent form is signed.

Subjects will be screened to determine eligibility for study enrollment. Subjects must meet all inclusion criteria and none of the exclusion criteria to participate in the study. All subjects screened will be documented on the Screening and Enrollment Log. Subjects who do not meet the eligibility criteria will be considered screen failures and the reason for the status of screen failure will be documented on the Screening and Enrollment Log.

[redacted]

6.4.3. Data Collection Procedure

6.4.3.1. The subject will be seated and/or lying-in supine position and should refrain from excessive movement during the study. Subject medical history and demographic information including age, sex, skin pigmentation, ethnicity, height, and weight may be recorded for data analysis and/or subject safety monitoring purposes.

[redacted]

6.4.3.3. INVSENSOR00057 will be placed on the subject's wrist according to the Investigator's Brochure. [redacted] The device may be repositioned, as needed, to ensure proper placement. The site of device placement should be assessed throughout the duration of the study. If there are any signs of loss of skin integrity and/or loss of circulation or perfusion, the device should be repositioned. In the unlikely event of emergency

defibrillation, the device must be removed prior to defibrillation.

6.4.3.4. [redacted]

6.4.3.5. Upon successful placement and Bluetooth pairing of the device, data collection will be initiated [redacted]

6.4.3.6. The subject will be requested to take manual ECG measurements on the INVSENSOR00057 [redacted]

6.4.3.7. Observations may be recorded on the case report form (e.g., subject position, timing and duration of manual measurements on the INVSENSOR00057 device).

6.4.3.8. At the conclusion of the procedure, the electrodes and device will be removed.

[redacted]

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 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 until completion of the study.
- A final close out visit after the last patient 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.

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 presence of informed consent, adherence to the inclusion/exclusion criteria, and documentation of SAEs/SADEs and protocol deviations/violations, and check CRF against source documentation.

After each visit, the monitor will provide a monitoring letter to the investigator within 4 weeks of visit completion. The monitoring letter 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 but no later than 60 days of receiving the monitoring letter. 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 patient safety, additional monitoring visits may be necessary according at the sponsor's discretion.

7. STATISTICAL DESIGN AND ANALYSIS

7.1. Acceptance Criteria

For validation studies, acceptance criteria are determined by Masimo specifications.

7.2. Sample Size

Analysis methods consistent with Receiver Operating Characteristics (ROC) curves will be used. Therefore, the sample size was determined to meet simultaneous requirements for both Sensitivity and Specificity. The PASS 2019 software package was used to calculate the appropriate sample size using the Confidence Intervals for One-Sample Sensitivity and Specificity module. [redacted]

7.3. Statistical Analysis

7.3.1. Exclusion

The following subjects will be excluded from data analysis:

- Subjects where the paired reference or test ECG did not provide readable ECG waveforms as determined by medical personnel.
- Subjects who presented as having Afib at the time of enrollment, but who provided ECG waveforms with characteristics inconsistent with an Afib diagnosis (as determined by medical personnel).

7.3.2. Afib Classification Accuracy Calculations

Classification accuracy will be measured by Sensitivity and Specificity as defined below.

Reference / Test	*AFIB*	*No AFIB*
AFIB	TP	FP
No AFIB	FN	TN

$$Sensitivity = \frac{TP}{TP + FN}$$

$$FalseAlarmRate = 1 - Specificity = \frac{FP}{FP + TN} = \frac{FP}{TotalNegativeEvents}$$

$$PPV = \frac{FP}{TP + FP} = \frac{FP}{TotalPositveDetections}$$

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN}$$

Analysis methods consistent with Receiver Operating Characteristics (ROC) curves will be used.

7.4. Expected Dropout Rates

Subjects may not complete the study for various reasons, such as a 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 per group 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: 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 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

- 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.
- No study-related activities will be conducted until the consent is signed and dated from the subject
- Following identification of a potential eligible subject as defined by the inclusion and exclusion criteria, the subject will be approached by the study staff. Study staff will explain the purpose and procedures of the study with respect to potentials risks and benefits, and clarification of the subject's rights and privacy information. The research team will emphasize that participation is voluntary and declining participation in the study will not result in any penalty or loss of benefits that the subject is otherwise entitled.
- Individuals will be given ample time to review the consent form and the opportunity to ask the person obtaining consent any questions.
- Once the subject's questions have been answered and the informed consent is signed and dated, the Principal Investigator or delegate will also sign the informed consent document, approving that the subject will be enrolled in the study. The investigator shall retain the original copy of the signed informed consent document in each subject's records and provide a copy to the subject.
- The point of enrollment is defined as the time at which the consent is signed and dated from the subject. The subject may withdraw from the study at any time.

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) foetal distress, foetal 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 will be reported and documented as described below.

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.
- Anticipated adverse events associated with the devices used in the study include:
    - Minor skin injuries, skin irritation, or skin sensitization
    - Potential pressure injury

- Subject discomfort

- 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 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 subjects require additional protection for the vulnerable population.

15.2. Protection of vulnerable subjects

- Reasonable compensation will be provided for economically disadvantaged subjects to eliminate possibility of undue influence due to financial incentive.
- Educationally disadvantaged 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.

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.

18. BIBLIOGRAPHY

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19. REVISION HISTORY

Version Number	Version Date	Summary of Revisions Made
[redacted]	[redacted]	[redacted]