Official Title: Calibration and Validation of the Masimo Rad-G with Temperature device in Febrile Patients

Date of Protocol: 24 January 2023

NCT Number: NCT05674344

Clinical Investigation Title: Calibration and Validation of the Masimo Rad-G with Temperature device in Febrile Patients

Clinical Investigation Number, Version:

Other Study Identifier: CHOC0008

Study Device(s): Masimo Rad-G with Temperature

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

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

IRB: CHOC Institutional Review Board –Research Institute
Address: 1201 W. La Veta
Orange, CA 92868

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

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

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

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

1. OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION

Clinical investigation title:	Calibration and Validation of the Masimo Rad-G with Temperature device in Febrile Patients
Study objective(s):	The objective of this study is to gather temperature data using the Masimo Rad-G with Temperature for calibration and validation purposes.
Investigational device(s):	Masimo Rad-G with Temperature
Number of participants:	Up to 250 participants.
Inclusion criteria:	• Participant age ≥ 1 year old • Febrile at time of enrollment: ≥ 99.5°F/37.5°C for sublingual temperature reference; ≥ 100.4°F/38°C for temporal artery temperature reference. • English- or Spanish-speaking patient or parent/Legally Authorized Representative (LAR)
Exclusion criteria:	• Participants deemed not suitable for the study at the discretion of the investigator • Patients who are rated as a 1 or 2 Emergency Severity Index
Duration of the clinical investigation:	The expected duration of study enrollment is 1 to 3 months.
Study endpoint(s):	[redacted] For the validation phase of the study, accuracy of temperature measurements using the Masimo Rad-G with Temperature will be compared to reference temperature measurements.

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.

The Masimo Rad-G with Temperature device (see Figure 1) is a non-contact infrared thermometry device [redacted] Non-contact infrared thermometers utilize infrared sensors that detect thermal radiation from the body. [redacted] The device is a non-invasive, non-contact, handheld pulse oximetry device with a rechargeable battery and LCD display. It uses Masimo Measure-through Motion and Low Perfusion™ SET® pulse oximetry technology to measure SpO2, respiration rate from the Pleth (RRp™), pulse rate (PR), perfusion index (PI), and temperature. The Masimo Rad-G is not FDA cleared and is considered investigational. Though the Rad-G may be used to measure the aforementioned parameters, the Rad-G used in this study will only be used to measure body temperature.

Figure 1: Masimo Rad-G with Temperature with integrated infrared temperature sensor at back of the device

[redacted]

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

This study is designed to be a two-phase calibration and validation study to obtain data for product development and clinical performance of the Masimo Rad-G with Temperature. [redacted] The second phase of the study will be the validation phase and will be used to evaluate the accuracy of temperature measurements using the Masimo Rad-G with Temperature.

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 participants; however, this study hopes to learn more about the temperature device to potentially help other patients in the future. Other possible benefits would be to society as a whole.

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

The Rad-G with Temperature device does not pose risks to the participant, because the device is non-contact and does not emit any energy. [redacted] using normal practice.

The other main risk associated with the study is a potential breach of confidentiality which will be minimized by limiting the collection of protected health information (PHI) and through secure data storage practices. None of our measures are diagnostic in nature. There is no other foreseeable risk associated with this study.

4.3 Importance of Knowledge Gained

Development of new temperature technologies could enable users to monitor temperature vital signs remotely and lessen the need for hospital visits.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

The objective of this study is to collect data for the calibration and validation of the Masimo Rad-G with Temperature to evaluate the performance of the device in obtaining temperature measurements. Measurements from the Masimo Rad-G with Temperature will be compared to [redacted]

6. DESIGN OF THE CLINICAL INVESTIGATION

6.1. General

This is a prospective, nonrandomized, single arm study. Temperature data will be obtained using the Masimo Rad-G with Temperature while obtaining [redacted]

There will be up to 250 participants enrolled into this study, divided into two groups: calibration and validation. [redacted] The second group will be the validation set that will be used to evaluate study objectives.

[redacted] For the validation phase of the study, accuracy of temperature measurements using the Masimo Rad-G with Temperature will be compared to [redacted]

The validation of the accuracy of the temperature measurement in the investigational device may be determined using data collected from this study, in addition to data from other Masimo sponsored studies.

6.2. Equipment and Materials

Equipment and materials are to be used as required. All study personnel will be trained on the use of relevant equipment.

Investigational Device

- Masimo Rad-G with Temperature

Reference Equipment (as needed)

[redacted]

- Hospital standard of care [redacted] thermometer
- Hospital grade [redacted] thermometer

Research Equipment

- Laptop with data collection software

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

The study will collect data to calibrate and validate the performance of the Masimo Rad-G with Temperature as compared to [redacted] measurements.

6.4. Participants

Inclusion Criteria

- Patients age ≥ 1year old
- Febrile at time of enrollment: ≥ 99.5ºF/37.5ºC for sublingual temperature reference; ≥ 100.4ºF/38ºC for temporal artery temperature reference.
- English- or Spanish-speaking patient or parent/LAR

Exclusion Criteria

- Patients deemed not suitable for the study at the discretion of the investigator
- Patients who are rated as a 1 or 2 Emergency Severity Index

6.5. Procedures

6.5.1. Recruitment and Pre-Screening

The principal investigator or delegated study personnel will screen for potential febrile participants in triage and/or review EMR current vital signs records for febrile participants in the emergency department. Patients who meet inclusion and exclusion criteria will be enrolled in the study.

6.5.2. Consenting and Screening

Per FDA Guidance "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects" issued on January 2017, waiver of documentation of informed consent for certain FDA-regulated minimal risk clinical investigations will facilitate investigators' ability to conduct studies that may contribute substantially to the development of products to diagnose or treat diseases or conditions, or address unmet medical needs. The IRB can waive the requirements to document informed consent when the IRB finds that:

- The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The clinical investigation could not practicably be carried out without the waiver or alteration;
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation

This study meets all the criteria listed by the FDA above and involves no more than minimal risk to the study participants because (1) the device under study is non-contact and (2) the clinical data to be obtained includes data collected for routine clinical use. The waiver is not expected to adversely affect the rights and welfare of the study participants because the study involves no-touch procedures and all data to be collected will be protected as outlined in the data collection and storage procedures. The clinical investigation could not practicably be carried out without the waiver due to the timing of the clinical assessment and immediate treatment of febrile conditions with antipyretics for children and adolescents in the Emergency Department.

After a caregiver/patient or their parent/LAR checks into the Emergency Department, a nurse or trained study investigator will approach them, and ask if they would like to participate in a short study looking at fever. If the patient or their parent/LAR is interested, an informational sheet outlining the study will be provided to them. This Study Information Sheet will be available in English and Spanish, the two most common languages in Orange County, California. The information sheet will be provided prior to the start of the study to inform the patient and/or their parent/LAR about the study and what data will be collected. Content on the information sheet will include: (1) research purpose and procedures, (2) risks, (3) benefits, (4) confidentiality, (5) whom (and how) to contact study personnel, (6) the voluntary nature of human research and the ability to withdraw participation, and (7) reporting of significant new findings. If the participant or their parent/LAR verbally agrees, they will be considered enrolled in the study. Verbal consent from the study investigator will be collected after review of the information sheet. Reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality is no greater than minimal. After having the opportunity to review the information sheet, study participants or their parent/LAR will have the opportunity to decline participation in the study. After participants have verbally consented, they will be entered into the study system and study procedures outlined in the protocol will proceed.

<u>HIPAA Waiver for Participant Screening</u>

The screening of participants will require the investigators to access personal health information to identify prospective participants without HIPAA authorization. The participants' rights and welfare will not be adversely affected by waiving HIPAA authorization. This protected health information will not be inappropriately reused or disclosed to any other person or entity. To further safeguard all protected health information, the data will not be labeled with any personal identifying information. Also, the data will not be stored with any protected health information identifiers.

6.5.3. Data Collection Procedure

6.5.3.1. Data collected by the Rad-G with Temperature is not intended to be used for clinical decisions, and research personnel should continue to use standard of care procedures for monitoring participants.

6.5.3.2. Study duration will be approximately 15 to 30 minutes.

6.5.3.6. Record start and end time of data collection procedures on the CRF.

6.5.3.7. Take the screening temperature measurement using the same thermometer to be used for the reference measurements, immediately before beginning the study measurements. The subject should be withdrawn from the study if they do not meet the criteria for temperature

Reference Measurements

Multiple reference measurements may be obtained.

6.5.3.12. The three measurements need to be taken in quick succession of each other, with approximately 3 seconds between each measurement

6.5.3.13. Be sure to keep the Rad-G device steady during the measurement.

[redacted]

6.5.3.15. In the validation phase, [redacted] measurements will be obtained per subject.

6.5.3.16. Data from the Rad-G with Temperature device will be downloaded using Masimo [redacted] software on the data collection laptop at the end of each day. Reference data [redacted] will be downloaded to the data collection laptop using a USB flash drive.

6.6. Monitoring plan

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

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

- An initiation visit, prior to any participant enrollment to confirm site readiness, and to document training on the study protocol and procedures, and use of equipment.
- At least one 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 participant 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 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

7.3. Sample Size

The minimum of 32 febrile patients for the validation phase per ISO 80601-2-56:2017, section 201.102.

7.4. Statistical Analysis

The statistical analysis will follow the procedure outlined in ISO 80601-2-56:2017 section 201.102.

7.4.1. Exclusion

Data from the following participants will be excluded from data analysis:

- Any subject administered antipyretic medications during study participation
- Any subject who does not complete at least one full round of measurements.
- Any subject whose data suggests a defective device or sensor.
- Any subject whose data suggests existence of external conditions that interfere with Rad-GT or reference measurements.

7.5. Expected Dropout Rates

Participants may not complete the study for various reasons, at the investigator's or study staff's discretion, or because the participant or participant's parent/LAR does not want to continue the study. Due to the short duration and simple, noninvasive procedures of this study, there are limited expected dropouts.

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

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

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

8.4. Data Transfer and Storage

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, 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 participants, 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 participant. Any unused devices must be returned to the Sponsor at the end of the study or before product expiration date.

11.3. Return or Destruction of Study Device

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

12. STATEMENTS OF COMPLIANCE

This document is a clinical investigational plan for a human research study sponsored by Masimo Corporation. The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. By participating in the study, the Investigator agrees to adhere to all stipulations of this protocol, the conditions of the Institutional Review Board (IRB) or Research Ethics Committee approval, federal and local regulatory requirements, 21 CFR 812, ISO-14155, International Conference on Harmonization Good Clinical Practice (ICH GCP) guidance.

The protocol, 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

A waiver of formal, written informed consent is requested because this study involves minimal risks and does not adversely affect participant rights and welfare. An information sheet will be provided at the start of the study to inform the patient/LAR about the study and what data will be collected. Verbal consent will be collected prior to study procedures. Reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality is no greater than minimal.

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

14.1. Definitions

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

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

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

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

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

  Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including 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. However, there are no anticipated adverse events as the

Rad-G with Temperature device does not pose risks to the participant, because the device is non-contact and does not emit any energy.

14.3. Adverse Event Reporting

- All Adverse Events, both Anticipated and Unanticipated, must be recorded in 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 populations are research participants, such as children, prisoners, pregnant women, handicapped, or mentally disable persons, or economically or educationally disadvantaged persons, who are likely to be vulnerable to coercion and undue influence. This study is targeting to enroll vulnerable populations such as children.

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

15.2. Protection of vulnerable participants

- For children, the Investigator will ensure that the parent/legal guardian does not unduly influence participants to participate. Parents/legal guardian of the participant will have ample time to ask questions about study devices and procedures.
- Educationally disadvantaged participants will be provided ample time to ask questions and comprehend information.
- Medical care will be provided to these participants after the clinical investigation has been completed if they are injured as a direct result of participating in this research study. The cost of treatment for any research related injury will be covered by Masimo.

15.3. Responsible Parties

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

16. SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

16.1. Suspension or Termination of Study Site

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

If the sponsor 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 participant enrollment upon receiving written notification of reinstatement from the sponsor.

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

16.2. Termination of Clinical Investigation/Study due to UADE

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

The sponsor may resume the terminated clinical investigation with prior 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 validation phase of the clinical investigation will be made publicly available.

18. BIBLIOGRAPHY

N/A

19. REVISION HISTORY

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