Official Title: Clinical Performance Testing of Philips FAST SpO_2 with Masimo Pulse Oximetry Sensors Across Skin Pigmentation

Date of Protocol: October 10, 2023

NCT Number: NCT06148623

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Clinical Investigation Number, Version: CIP-1088 Revision [redacted]

Other Study Identifier: N/A

Study Device(s): Philips FAST SpO_2
Masimo Pulse Oximetry Sensors

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

Sub-Investigator: [redacted]

Investigation Site(s): Clinical Laboratory, Masimo Corporation

Address: 52 Discovery
Irvine, CA 92618

IRB: [redacted]

Address: [redacted]

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 to prior to enrollment, per FDA (Food & Drugs Administration) 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 determine 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 the 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:	Clinical Performance Testing of Philips FAST SpO_2 with Masimo Pulse Oximetry Sensors Across Skin Pigmentation
Study objective(s):	The primary objective of this study is to validate the performance of Philips FAST SpO_2 with Masimo Pulse Oximetry Sensors in determining functional arterial oxygen saturation (SpO_2) using arterial saturation (SaO_2) as a reference in the range of 70-100% in subjects of varying skin pigmentation. The secondary objective of this study is to determine the difference between three population subgroups for light, medium, and dark skin pigmentation.
Investigational device(s):	Philips FAST SpO_2 with Masimo Pulse Oximetry Sensors
Number of subjects:	Minimum 24 subjects.
Inclusion criteria:	Refer to section 6.3.1.
Exclusion criteria:	Refer to section 6.3.2.
Duration of the clinical investigation:	Expected duration of study enrollment is 1 to 3 months. Subject participation in the study will be approximately 180 minutes.
Study endpoint(s):	Primary end point: Philips FAST SpO_2 with Masimo pulse oximetry sensors meets its performance specifications. Secondary end point: Report the difference between the A_{RMS} for the skin pigmentation subgroups (light, medium, and dark)

2. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

2.1. Technology Background

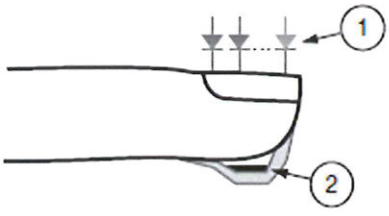
Pulse oximetry technologies

Pulse oximeters use light-emitting diodes (LEDs) to pass light through a site to a photodiode (detector) (Figure 1).

Pulse oximetry is governed by the following principles:

Oxyhemoglobin (oxygenated blood) and deoxyhemoglobin (non-oxygenated blood) differ in their absorption of red and infrared light (spectrophotometry).

The amount of arterial blood in tissue changes with arterial pulses. Therefore, the amount of light absorbed by the varying quantities of arterial blood changes as well and this can be used for photoplethysmography.



1. Light Emitting Diodes (LEDs) (2+ wavelengths)
2. Detector

Figure 1: Pulse Oximeter LED and Detector locations.

2.2. Study Device(s)

Philips FAST SpO_2

Philips FAST SpO_2 (Fourier Artifact Suppression Technology) applies an algorithm that examines the signal in the frequency domain. This technology is used as a platform (picoSAT) in certain variants within many different Philips devices. Each device using one of the platform variants (e.g., IntelliVue X3) can be used in a desaturation study as a representative for the others.

Pulse Oximeter Sensors and Cables

Masimo rainbow SET and SET noninvasive pulse oximeter sensors vary in the number of LEDs and supported parameters. The sensors may also differ in the design compatibility to different sensor application factors, such as securement means (i.e., finger clips or adhesive) and patient population (e.g., adults, neonates, infant, and pediatrics).

2.3. Site Information

The Masimo Clinical Laboratory facility is designed as [redacted] clinical study research center. The laboratory is staffed by [redacted] All personnel undergo routine required training on Good Clinical Practice (GCP) and human research subject protections. The laboratory is equipped with [redacted] In case of emergencies, hospitals and urgent care facilities are within three miles of the Masimo Clinical Laboratory.

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

This study is designed to test the performance of Philips FAST SpO_2 with Masimo pulse oximetry sensors as the subjects undergo a controlled desaturation protocol. This type of study design is required to test the performance of pulse oximeters in accordance with the ISO-80601-2-61:2017 standard for pulse oximeters, which is also adopted and referenced by the FDA for pre-market submissions.

Data will be collected from male and female study subjects representing various skin pigmentations. [redacted]

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

4.1. Anticipated Benefits

There will be no benefit to the subject. Benefits would be to society as a whole. Evaluation of the performance of new devices 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 considered anticipated adverse events. All adverse events will be documented and reported according to Section 14.3.

- **Risks Associated with the Sensors/Devices**

The noninvasive and minimally invasive devices used in this study are similar in technology and design to some commercially available pulse oximeters and other non-invasive/minimally invasive devices and hence have the same minimal risks.

Risks associated with sensors/devices include but are not limited to damage to the subject's fingers, or other locations where sensors are placed, including temporary skin irritation or discomfort associated with exposure

to the sensor, temporary mechanical irritation or discomfort, sensor burn with a potential for permanent skin damage (e.g., scar, discoloration), injury from tripping over or entanglement in sensor cables.

If there are any cuts or abrasions near the fingernail, certain types of sensors may not be placed on the particular finger to avoid any discomfort for the subject.

- **Risks Associated with Skin Preparation**

  Risks associated with the skin preparation include but are not limited to cuts, abrasions, rash, itching skin, flushing or redness of the skin, unusually warm skin, skin inflammation, and skin irritation. Each of these discomforts and side effects are temporary and should improve over time.

  If there are any cuts 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.

[redacted]

- **Risks Associated with Adhesives**

  Risks associated with adhesives include but are not limited to skin irritation, redness of the skin, skin inflammation, itchiness, swelling, tingling sensation, rash, changes in skin color, and headache.

  Subjects who are allergic to adhesives will be excluded from participation in this study.

- **Risks Associated with Lidocaine Injection**

  Risks associated with lidocaine injection include discomfort, pinching sensation, warm/burning sensation, pain, flushing or redness of the skin, itching skin, small red or purple spots on the skin, unusually warm skin, bruising, bleeding at the application site, swelling, feeling nauseated, dizziness, low blood pressure, and tremors.

  Although not common, it is also possible to have an allergic reaction to injectable lidocaine. Subjects should not take part in this study if they are allergic to lidocaine injection or other types of numbing medicine, or if they have a heart rhythm disorder such as Wolff-Parkinson-White Syndrome or Stokes-Adams Syndrome. Subjects are instructed to tell the study staff right away if they experience any discomfort including hives, difficulty breathing, and swelling of the face, lips, tongue, or throat, or seizures.

- **Risks Associated with Skin Refrigerant (e.g., Pain Ease, Ethyl Chloride)**

  Risks associated with skin refrigerant include but are not limited to changes in skin color (e.g., flushing or redness of the skin), delayed wound healing, rash, itching, and swelling.

- **Risks Associated with Venous Blood Draw**

  Risks associated with venous blood draw include discomfort, pain, bruising or hematomas, infection, tendon or tissue damage, damage to the blood vessel and surrounding nerves, inadvertent arterial puncture, and loss of feeling in the hand or arm.

  Additional risks include but are not limited to vasovagal syncope (fainting), lightheadedness, feeling flush/warm, feeling pain, feeling nauseated, throwing up, seizures, sudden drop/increase in blood pressure, sudden drop/increase in heart rate, blood loss, tingling sensation of face or extremities, sweating, and/or mouth dryness.

- **Risks Associated with Venous Cannulation**

  Risks associated with venous cannulation include discomfort, pain, bruising, bleeding, swelling, infection, hematoma, decreased blood supply, damage to the blood vessel and surrounding nerves, tendons, or tissue, and loss of feeling in the hand and/or arm.

  Additional risks include but are not limited to vasovagal syncope (fainting), infiltrated IV, blood clot, lightheadedness, feeling flush/warm, feeling nauseated, throwing up, seizures, sudden drop/increase in blood pressure, sudden drop/increase in heart rate, tingling sensation of face or extremities, sweating, mouth dryness, and injury from tripping over or entanglement in lines.

- **Risks Associated with Arterial Cannulation**

  Risks associated with arterial cannulation include discomfort, pain, bleeding, decreased blood supply, swelling, infection, bruising, hematoma, and damage to the blood vessel and surrounding nerves, tendons, or tissue.

  Additional risks include but are not limited to pain, vasovagal syncope (fainting), lightheadedness, feeling flush/warm, embolization (blood clot), feeling nauseated, throwing up, seizures, sudden drop/increase in blood pressure, sudden drop/increase in heart rate, irregular heart rate (e.g., premature atrial contraction (PAC), premature ventricular contraction (PVC), ECG abnormalities), tingling sensation of face or extremities, sweating, mouth dryness, arterial occlusion, arterial laceration, loss of feeling in the hand and/or arm, loss of the hand and/or arm due to rare complications of arterial cannulation, and injury from tripping over or entanglement in lines.

- **Risks Associated with a Mask, Nasal Cannula, or Mouthpiece**

  Risks associated with a mask, nasal cannula, or mouthpiece include but are not limited to irritation, redness, congestion, pressure, indentations on the skin, feelings of claustrophobia or anxiousness, and injury from tripping over or entanglement in lines or tubing.

- **Risks Associated with a Nose Clip**

  Risks associated with a nose clip include but are not limited to discomfort, pinching, scratches, indentations, and symptoms similar to a headache.

- **Risks Associated with Low Oxygen Concentration (Hypoxia)**

  Risks associated with low oxygen concentration include lightheadedness, dizziness, shortness of breath, drowsiness, or headache. If these symptoms occur, the study can be stopped.

  There is an extremely small risk of loss of consciousness or death from lack of oxygen. The study shall be stopped by the subject or clinical staff long before this could occur.

  Breathing a hypoxic (reduced oxygen) mixture has potential risks that include damage to vital organs such as the brain, liver, kidney and/or heart. Note that several studies have been done with low oxygen using generally healthy subjects without any serious or permanent damage to any of the major organs.

  Additional risks include but are not limited to vasovagal syncope (fainting), chest discomfort (e.g. chest tightness, chest pain), feeling flush/warm, feeling of anxiety, feeling nauseated, throwing up, seizures, sudden drop/increase in blood pressure, sudden drop/increase in heart rate, irregular heart rate (e.g., premature atrial contraction (PAC), premature ventricular contraction (PVC), ECG abnormalities), tingling sensation of face or extremities, sweating, mouth dryness, feeling claustrophobic or anxiousness from wearing a mask/mouthpiece.

- **Risks Associated with Oxygen Administration**

  Risks associated with oxygen administration include but are not limited to dryness, cough, congestion, throat or chest irritation, mucosal irritation, or nose bleeds.

  Risks associated with high flow/pressure oxygen administration [redacted] include but are not limited to moderate carinal irritation on deep inspiration after 3-6 hours of exposure, extreme carinal

irritation with uncontrolled coughing after 10 hours, and chest pain and dyspnea after more than 10 hours.
[redacted]

- **Risks Associated with Carbon Dioxide Administration**

  Risks associated with carbon dioxide administration include lightheadedness, dizziness, shortness of breath, drowsiness, or headache. If this occurs, the study can be stopped.

  Additional risks include but are not limited to dryness, cough, congestion, throat or chest irritation, mucosal irritation, nose bleeds, tingling, prickling sensations ("pins and needles" feeling), restlessness, sudden drop/increase in blood pressure, sudden drop/increase in heart rate, irregular heart rate (e.g., premature atrial contraction (PAC), premature ventricular contraction (PVC), ECG abnormalities), and sweating.

[redacted]

4.3. Emergency Response Plan for Medical Emergencies

[redacted]

[redacted]

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

4.4. Alternatives

The alternative is for the subject to not participate in the study.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

5.1. The primary objective is to test the performance of Philips FAST SpO_2 with Masimo pulse oximetry sensors in measuring functional arterial oxygen saturation (SpO_2) using an arterial saturation (SaO_2) reference in the range of 70-100% in subjects of varying skin pigmentation.

The secondary objective of this study is to determine the difference in performance between three population subgroups for light, medium, and dark skin pigmentation.

5.2. Outcome Measure:

Performance will be determined by calculating the A_{RMS} comparing the noninvasive oxygen saturation measurement (SpO_2) to the arterial oxygen saturation (SaO_2) value obtained from a reference blood sample.

A_{RMS} will also be computed for each pigmentation subgroup, and the difference between the subgroup A_{RMS} will be calculated.

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 receive the Masimo pulse oximeter sensor on at least one finger. Desaturations will be conducted by reducing the concentration of oxygen the study subject breathes in a controlled manner to obtain noninvasive oxygen saturation readings of SpO_2, at various levels.

Reference blood samples will be repeatedly collected from the subject and analyzed using a calibrated laboratory CO-oximeter. The performance will be calculated using an Accuracy Root Mean Square (A_{RMS}) analysis of the SpO_2 values to the reference SaO_2 values from a CO-oximeter.

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 (e.g., skin pigmentation, race/ethnicity, age, gender) 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's specifications and all study personnel will be trained in the use of relevant equipment.

Safety Equipment (FDA-Cleared)

[redacted]

Test Devices

- Philips FAST SpO_2
- [redacted] Masimo Pulse Oximetry Sensors [redacted]

Research Equipment

[redacted]

6.1.4. Standard Safety Precautions

[redacted]

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.

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

The investigational device is the combination of the Philips FAST SpO_2 with Masimo Pulse Oximeter sensors. The Masimo Pulse Oximeter sensors are cleared sensors that do not pose any additional risks.

The reference is an arterial blood sample. [redacted]

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 18 to 50 years of age.
- Subject weighs a minimum of 110 lbs.

- Baseline heart rate ≥ 45 bpm and ≤ 90 bpm.
- Blood Pressure: Systolic BP ≤ 140 mmHg and ≥ 90 mmHg, Diastolic BP ≤ 90 mmHg and ≥ 50 mmHg, and if systolic BP is lower than 100 mmHg and/or diastolic BP is lower than 60 mmHg, subject passes an orthostatic blood pressure test.
- Hemoglobin value ≥ 11 g/dL.
- CO value ≤ 3.0% FCOHb.
- Subject can read and communicate in English and understands the study and the risks involved.

6.3.2. Exclusion Criteria (Ineligible Subjects) (* = per clinician discretion)

- Subject is pregnant or breastfeeding.
- Subject has a BMI > 35.
- Subject has a history of fainting (vasovagal syncope), blacking out or losing consciousness during or after a blood draw, or has a fear of blood draws.
- Subject has open wounds, inflamed tattoos, or piercings, and/or has any visible healing wounds that a medical professional determines may place them at an increased risk for participation. *
- Subject has finger deformities, nail deformities, nail polish, and/or gel/acrylic that can interfere with study device placement. *
- Subject has known drug or alcohol abuse.
- Subject uses recreational drugs. *
- Subject experiences frequent or severe headaches and/or migraine headaches, migraine auras, altitude sickness, and/or headaches accompanied by visual changes or sensitivity to light or sound.
- Subject has experienced a concussion or head injury with loss of consciousness within the past 12 months.
- Subject has any history of a stroke, myocardial infarction (heart attack), and/or seizures.
- Subject has any chronic bleeding disorder (e.g., hemophilia).
- Subject has taken anticoagulant medication within the past 30 days (excluding nonsteroidal anti-inflammatory drugs (NSAIDs)).
- Subject has donated blood within the past 4 weeks.
- Subject has any cardiac dysrhythmia (e.g., atrial fibrillation) and has not received clearance from their physician to participate.
- Subject has a known neurological and/or psychiatric disorder (e.g., schizophrenia, bipolar disorder, Multiple Sclerosis, Huntington's disease) that interferes with the subject's level of consciousness. *
- Subject has taken opioid pain medication 24 hours before the study.
- Subject has any infectious disease (e.g., Hepatitis, HIV, Tuberculosis, Flu, Malaria, Measles). *
- Subject is taking medications known to treat any type of infectious disease.
- Subject has either signs or history of peripheral ischemia or carpal tunnel syndrome.
- Subject has had invasive surgery within the past year, including but not limited to major dental surgery, appendectomy, plastic surgery, jaw surgery, major ENT surgery, major abdominal and/or pelvic surgery, heart surgery, or thoracic surgery. *
- Subject has symptoms of congestion, head cold, or other illnesses.
- Subject has been in a severe car accident(s) or a similar type of accident(s) requiring hospitalization within the past 12 months.
- Subject has any cancer or history of cancer (not including skin cancer). *
- Subject has chronic unresolved asthma, lung disease (including COPD) and/or respiratory disease.

- Subject is allergic to lidocaine, chlorhexidine, latex, adhesives, or plastic.
- Subject has a heart condition, insulin-dependent diabetes, uncontrolled hypertension, or hypercholesterolemia.
- Subject delivered vaginally, had a pregnancy terminated, had a miscarriage with hospitalization, or had a C-section within the past 6 months.
- Subject intends on participating in any heavy lifting, repetitive movement of their wrist (including riding a motorcycle, tennis), exercise (e.g., working out, riding a bike, riding a skateboard), or any activity that will put additional stress on the wrist within 24 hours following a study that involves an arterial line.
- Difficulty inserting an intravenous line in the subject's hand or arm and/or an arterial line in the radial artery of the subject's wrist.
- Subject has any medical condition which in the judgment of the investigator and/or medical 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

[redacted] The expected duration of each subject's participation in the lab will be approximately 180 minutes. In the event that the total overall lab time exceeds 180 minutes, subjects will be compensated for the additional time.

6.3.4. Withdrawal of Subjects

Subjects must be withdrawn under the following circumstances: the subject withdraws consent, or at the discretion of investigator/study staff for subject safety and welfare.

6.3.5. Replacement of Subjects

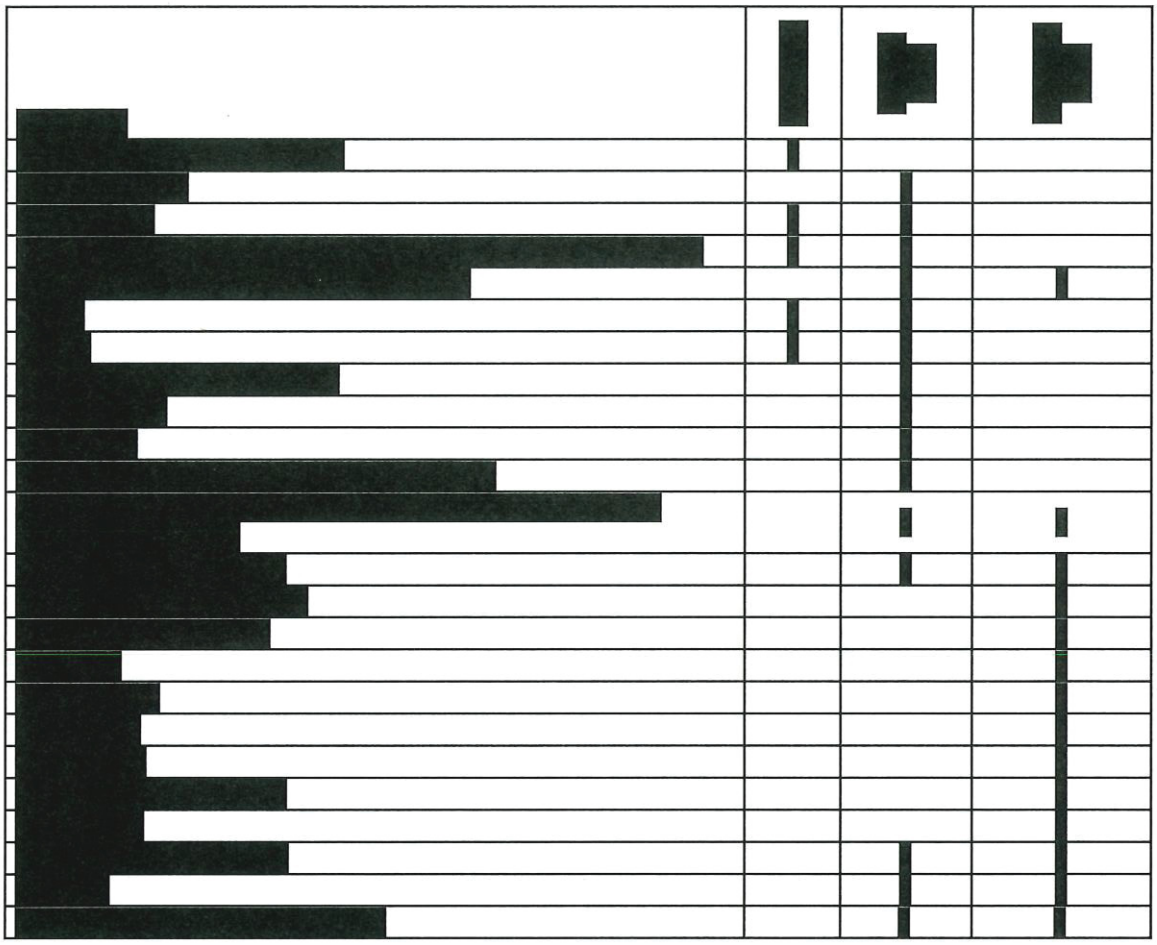
In case a subject is withdrawn from the study, another subject may be recruited.

6.3.6. Re-contacting Subjects

If the subject fails to provide proper documentation on their individual consent form or other study documents, Masimo may re-contact the subject and ask them to return to the clinical lab to properly complete these documents. The subject will be re-contacted via phone or email and be asked to return as soon as possible. The subject will be compensated for travel as outlined in the consent form.

6.4. Procedures

6.4.1. Schedule of Activities



6.4.2. Recruitment and Pre-Screening

6.4.2.1. Advertisement and Recruitment

Recruitment materials are posted [redacted]. We will recruit human subjects, which will include members of the general public [redacted]

Subjects of various levels of skin pigmentation will be enrolled in the study. Skin pigmentation data from prior study participation may be used to recruit subjects.

6.4.2.2. Subject Screening

Once the potential subject sees the recruitment material [redacted] they can contact us to inquire about more details about the study.

Screening for subject eligibility will be completed by research staff [redacted]

[redacted]

[redacted]

Information from the screening will be kept [redacted] The information is kept to contact subjects for other studies they may qualify for or for instance, to track subjects who call in and provide false information only to qualify.

6.4.3. Consent, Health Assessment, Eligibility Determination, General Procedures

Subjects may be asked to provide a copy of their valid government photo ID and/or Social Security Number card (SSN) to verify subject information in our scheduling database and/or to verify the subject's identity. A W-9 form may 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 as verification of subject identities or to track subjects who provide false identification.

Subjects must read and sign the consent document, using our informed consent process. A copy of the signed consent document will be retained (either on paper or electronically). No study-related activities will be conducted until the consent form is signed.

Subjects will be asked if they consent to photography, videography, audio recording, or presence of an observational group during the study. [redacted] No recordings will be obtained without the subject's consent. If a subject does not consent to photography, videography, audio recording, or an observational group, the subject may still proceed in the study.

Subject demographic information will be collected (and may include but is not limited to age, sex, skin tone, ethnicity, race, height, weight, and finger size, and ear size). These may be recorded for data analysis and/or subject safety monitoring purposes. Skin pigmentation may be assessed using [redacted]

Skin pigment may be assessed at the following sites: [redacted] Measurements will include [redacted]

Body mass index (BMI) may also be calculated to assess eligibility for the study.

Female subjects/subjects with childbearing potential will be required to take a pregnancy test. Results will be noted. If the pregnancy test is positive, the subject will be removed from the study and notified of their pregnancy test results.

In addition, a medical history will be recorded after the initial screening questionnaire. Vital signs, such as blood pressure and heart rate, will be recorded for subject safety monitoring. Pulse oximetry measurements, such as SpO_2, SpCO, and SpHb, may also be recorded.

[redacted]

[redacted]					

[redacted]

A venous blood sample will be obtained and analyzed to verify that the starting hemoglobin level is greater than or equal to 11.0 g/dL and carboxyhemoglobin (COHb) level is less than or equal to 3.0%. If hemoglobin level is less than 11.0 g/dL and/or COHb is greater than 3.0%, the subject will be excluded from the study.

After testing, blood samples will be de-identified and discarded in the appropriate biohazard waste bins.

[redacted]

Subjects may be offered a snack (e.g., granola bar) and/or beverage (e.g., water, juice) due to the amount of time their involvement in this study may take.

6.4.4. Line Placement and Sensor Placement

[redacted]

Standard noninvasive monitors will be placed on the subject when preparing for study procedures, which may include FDA-cleared pulse oximeters, ECG, and blood pressure cuff(s) (may not be recorded automatically depending on the protocol, this may be recorded manually for monitoring by medical staff). This is assessed for subject monitoring only. Blood pressure may be obtained from arm cuffs, leg cuffs, finger cuffs, or equivalent devices. Blood pressure may be taken manually or automatically depending on the device used. [redacted]

[redacted]

Transient increases in blood pressure and heart rate can be expected during line placement, needle sticks, blood draws, etc. and may also be attributed to anxiety/nervousness relating to a new environment. For most participants, only the initial recorded blood pressure and/or heart rate determines a subject's qualification for the study. In the case where heart rate and blood pressure changes suggest participant discomfort or a potential safety concern, the participant will be removed from the study after qualifying, according to the discretion of medical and study staff.

A peripheral venous line may be placed in the subject's hand or arm for safety purposes. One or more venous sampling catheters may be used during the study for removal of samples of blood to allow for determination of venous oxygen saturation as well as other non-infectious blood solutes. This line may be used for a qualifying blood draw to verify that the participant meets inclusion criteria. The peripheral venous line site will be observed by study staff prior to line placement to ensure no bruising remains from any previous IV placements; if there is bruising the clinician will place the line in another location.

Local anesthetics such as Lidocaine, ethyl chloride spray, or Pain Ease skin refrigerant spray may be used in the event that an IV is placed to numb the site. Subjects will be given the option to have lidocaine or numbing spray be used during IV placement for the purpose of making catheter placement more comfortable for the subjects.

After intravenous access (if necessary) is established, one or more intra-arterial catheter(s) (arterial line or A-line) may be placed in the radial artery of the subject's wrist. This study is being done with an arterial line to facilitate continuous blood sampling to determine arterial blood gas values (ABG), such as oxygen saturation, as well as other non-infectious blood solutes.

[redacted]

Upon successful placement of the IV(s) and the subject's indication that they are comfortable, a minimum of one FDA-cleared pulse oximeter sensor may be placed on the subject for reference values such as, but not limited to, oxygen saturation, total hemoglobin, carbon monoxide, and pulse rate.

[redacted]

Other standard output parameters may also be recorded from the device(s) (e.g., SpO_2, pulse rate, perfusion index, signal quality data).

6.4.5. Hypoxia (Desaturation) Procedure

Oxygen tank pressure will be checked and noted before the study begins for subject safety purposes.

[redacted]

Subjects may use a mask during the desaturation procedure. [redacted]

End-tidal and/or partial pressure of carbon dioxide and respiration rate values will be noted at the beginning of the desaturation portion of the study for subject safety purposes and will be noted again at the end of the desaturation portion of the study. [redacted] Upon indication that the subject is comfortable, a gas mixture will be administered. The gas mixture may include varying proportions of oxygen, carbon dioxide, and nitrogen. The proportion of oxygen in this mixture will be decreased to lower the subject's blood oxygen saturation. The lowest targeted value will be 70% oxygen saturation [redacted] Note: At any point in the study, if the subject feels uncomfortable, the subject will be given oxygen through a mask or nasal cannula.

A qualified person will complete blood draws [redacted]

[redacted]

[redacted]

The study will end with a FiO_2 greater than or equal to room air (21%) to help the subject re-saturate after the procedure. If at any point the subject is uncomfortable with the study, the study will be stopped.

6.4.6. Ending Procedure

The total overall lab time will be approximately 180 minutes. In the event that the total procedure time exceeds 180 minutes, subjects will be compensated for the additional time.

At the conclusion of the procedure, the sensor(s)/device(s), and IV(s) will be removed. A set of pre-discharge vitals, such as heart rate and blood pressure, will be obtained and recorded on the case report form for subject safety purposes. The subject will be allowed to leave after medical personnel determine it is safe to do so.

[redacted]

All subjects will be encouraged to remain in the study area until they feel fit to leave. Subjects should feel safe and able before returning to work directly after participation in the study. [redacted]

Subjects will be given instructions on post care. All subjects will be instructed to contact the principal investigator and/or study staff in the event of any potential complication.

[redacted]

After the study has ended subjects will be offered a snack (e.g., granola bar) and something to drink (e.g., water, juice). Subjects may be asked to consume the food and/or liquid prior to leaving the clinical lab area for their safety due to study procedures such as blood removal and line placement. Subjects may also be asked to wait in the clinical lab or lobby waiting area for approximately 20 minutes before leaving to allow for their body to continue adjusting after the study has completed.

6.5. Monitoring plan

[redacted]

7. STATISTICAL DESIGN AND ANALYSIS

7.1. Acceptance Criteria

The Philips FAST SpO_2 with Masimo Pulse Oximetry Sensors shall meet its labeled Arms specifications.

7.2. Sample Size

[redacted]

c. [redacted] This study will target a minimum of 24 subjects but may be modified based on actual numbers required to maintain adequate power for the study.

d. Depending on dropout rates, additional subjects may be enrolled to obtain sufficient representative data for factors such as gender, skin pigmentation, oxygen saturation, and other factors as required.

7.3. Statistical Analysis

a. The final A_{RMS} analysis will utilize statistical methods to ensure performance statistics are calculated with comparable density over the range 70-100% SaO_2 and account for multiple samples per subject.

b. Statistical analysis for each subgroup will be performed to show differences in biases among different subgroups.

c. Exclusions

The following data exclusion criteria will be applied before statistical analysis:

i. Either reference or test device does not provide data.

ii. Incomplete study or early termination, where the desaturation protocol could not be completed.

[redacted]Reference device malfunctions [redacted]

iv. Discontinuities and abrupt dropouts due to instruments recalibration or device failure.

[redacted]Low signal quality, e.g. due to noise or interference. [redacted]

[redacted]Subject's oxygen saturation is unstable. [redacted]

vii. Exclusion of subjects that do not have desaturation points in the lowest saturation bin (70-80%).

viii. Exclusion of data to statistically equalize samples per subject, and across the 70-100% saturation bins.

d. Accuracy calculations

Accuracy will be reported as the Mean Bias, Precision, and A_{RMS} using the following equations:

$$Mean\ Bias = \frac{1}{n}\sum_{i=1}^{n}(SpO_{2i} - SaO_{2i})$$

$$\text{Precision} = \sqrt{\frac{\sum_{i=1}^{n}\left(SpO_{2i} - SpO_{2ifit}\right)^2}{n-2}}$$

[redacted]

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

The A_{RMS} will be adjusted to account for repeated measurements on each subject.

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.

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 of 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 include/ 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 the study monitors during site visits.

8.4. Data Transfer and Storage

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

secure server.

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

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

8.5. Record Retention

Study data will be retained for the necessary period as required by the institution's regulations. Study records shall be retained for a minimum of 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 from each shipment will be documented in the study files. The investigator must notify the study sponsor of any damaged or unusable study devices that were supplied to the investigator's site.

11.2. Use of Study Device

Use of device will be documented on case report forms for each subject. Any unused devices must be returned to the Sponsor at the end of the study or before the product's 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 the 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

Subjects must read and sign the consent document using the informed consent process as outlined in [redacted] 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 14155-1, 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 related to the investigational medical device and whether anticipated or unanticipated (ISO 14155-1)
- 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 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 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 also be 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 (about 2 days). All other Adverse Events should be reported to the Sponsor within 5 business days.
- All Serious Adverse Events will also be 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 disabled 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

[redacted]

- Reasonable compensation will be provided for economically disadvantaged subjects to eliminate the possibility of undue influence due to financial incentive.
- Educationally disadvantaged subjects will be provided with 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 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 determines that the study site's compliance to be inadequate at any point during the study, and sponsor moves 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 recur in the future. The 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

ISO-80601-2-61:2017 Medical electrical equipment -- Particular requirements for the basic safety and essential performance of pulse oximeter equipment for medical use.

[redacted]

19. REVISION HISTORY

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