Official Title: Clinical Performance of INVSENSOR00040

Date of Protocol: March 14, 2023

NCT Number: NCT05332392

Clinical Investigation Title: Clinical Performance of Masimo INVSENSOR00040

Clinical Investigation Number, Version:

Other Study Identifier: N/A

Study Device(s): Masimo INVSENSOR00040 – Investigational

Sponsor: Masimo Corporation
52 Discovery
Irvine, California 92618 USA

Investigator Page

Principal Investigator (s): [redacted]

Investigation Site(s): Masimo Corporation – Clinical Lab
Address: 52 Discovery
Irvine, CA 92618

IRB: E&I West Coast Board – IRB00007807

Address: 304 SE 3rd Street
Lee's Summit, MO 64063

Agreement between Investigator and Sponsor Regarding Responsibilities for Good Clinical Practice

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

It specifies general requirements intended to:

- Protect the rights, safety and well-being of human subjects,
- Ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- Assist sponsors, monitors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

The Principal Investigator of the clinical investigation shall:

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

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

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

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

1. OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION

Clinical investigation title:	Clinical Performance of Masimo INVSENSOR00040
Study objective(s):	The primary objectives: 1. Validate performance of the Masimo INVSENSOR00040 functional arterial oxygen saturation (SpO2) on a diverse subject population during no motion conditions across an arterial saturation (SaO2) range of 70-100%. 2. Validate performance of the Masimo INVSENSOR00040 Pulse rate (PR) within its specified range on a diverse subject population during no motion conditions while undergoing desaturations protocols. [redacted]
Investigational device(s):	Masimo INVSENSOR00040
Number of subjects:	A minimum of 25 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 3 to 6 months. Subject participation in the study will be approximately 180 minutes.
Study endpoint(s):	Validation of the SpO2, PR [redacted] performance of INVSENSOR00040

2. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

2.1. Background and Study Devices

An invasive blood sample analyzed by a CO-oximeter reference instrument gives the best measure of arterial oxygen concentration as well as other blood solutes but cannot measure these parameters continuously and requires skin puncture, arterial line placement and subsequent risk of infection, hematoma, and other physiological damage.

Masimo Corporation develops non-invasive medical technologies. These devices have applications in the operating room, critical care unit, emergency room, emergency transport vehicles, alternative (home) care, as well as physicians' offices. Masimo SET, Masimo rainbow, and other newly developed Masimo technology allow real-time, non-invasive monitoring of oxygen saturation. Use of monitoring devices on patients has the potential to improve clinical outcomes while reducing the cost of care and risks to both patients and clinicians associated with arterial and venous punctures.

The investigational INVSENSOR00040 used in this study is similar to the commercially available wearable health monitoring devices except that it has a continuous SpO2 (functional oxygen saturation) function. Masimo INVSENSOR00040 is a stand-alone 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 is capable of calculating SpO2 and pulse rate (PR)[redacted] as well as other pulse oximeter parameters (e.g. perfusion index, etc.).

Masimo INVSENSOR00039 and/or other FDA-cleared or other commercially available pulse oximeters may be used for research purposes.

2.2. Site Information

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

3. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

This study is designed to compare the performance of the INVSENSOR00040 as the subjects undergo a controlled desaturation protocol. This type of study design is required to evaluate the performance of pulse oximeters based upon the ISO 80601-2-61 standard which is also adopted and referenced by the FDA.

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

4.1. Benefits:

There will be no benefit to the subject. Other possible benefits would be to society as a whole. Evaluation of the accuracy of this new device could enable users to more appropriately monitor and identify potentially life-threatening conditions.

4.2. Risks/Discomforts:

- **Device Risks:**

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

  There is a small risk of temporary skin irritation or discomfort associated with exposure to the sensor, as well as potential temporary mechanical irritation or discomfort from the wrist band. There is a remote, yet possible, risk of a burn from the sensor. In the case of a sensor burn, there is the potential for permanent skin damage (scar/discoloration).

  If there are any cuts and/or abrasions near the application wrist, subject will disqualified from study to avoid any discomfort.

- **Venous Cannulation Risks:**

  Risks associated with venipuncture include discomfort, 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.

  Other anticipated adverse events that may occur, include but are not limited to: vasovagal syncope (fainting), infiltrated IV, blood clot, lightheadedness, feeling flush/warm, feeling pain, feeling nauseated, throwing up, seizures, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, tingling sensation of face, arms and/or legs, sweating, and/or mouth dryness.

  These anticipated adverse events are expected to be temporary.

- **Arterial Cannulation Risks:**

  Risks include bleeding, decreased blood supply, swelling, infection, bruising, hematoma, damage to the blood vessel and surrounding nerves, tendons, or tissue. Additional risks include vasovagal syncope (fainting), lightheadedness, feeling flush/warm, feeling pain, embolization (blood clot), feeling nauseated, throwing up, seizures, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, irregular heart rate (PAC, PVC, EKG abnormalities, etc.), tingling sensation of face, arms, and/or legs, sweating, mouth dryness, arterial occlusion, arterial laceration, loss of feeling in the hand and/or arm, and even the loss of the hand due to rare

complications of the study.

- **Blood Draw Risks:**

  Discomfort is generally associated with needle puncture. The most common complications associated with blood draws are hematomas or bruising. There is also a possible risk of infection, tendon or tissue damage, damage to the blood vessel and surrounding nerves, inadvertent arterial puncture, and/or loss of feeling in the hand and/or arm.

  Other anticipated adverse events that may occur, include but are not limited to: vasovagal syncope (fainting), lightheadedness, feeling flush/warm, feeling pain, feeling nauseated, throwing up, seizures, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, tingling sensation of face, arms and/or legs, sweating, and/or mouth dryness. These anticipated adverse events are expected to be temporary.

- **Risk from Oxygen Administration:**

  It is expected that some people may experience feelings of claustrophobia or anxiousness from wearing a mouthpiece, mask, and/or nasal cannula. There are no additional risks associated with high oxygen/oxygen administration for less than 24 hours as long as subjects do not have any cardiac conditions, COPD or any other lung diseases.

  Subjects' answers on the health questionnaire will help the medical staff decide if they can safely participate in this study; subjects are encouraged to let the study staff know if they have any concerns.

- **Risk from Mask Application:**

  A mask may be applied to the subject's face using an adhesive dressing or using straps. Risks associated with mask adherence include skin irritation, redness of the skin, itchiness, tingling sensation, rash, changes in skin color, and/or headache. It is expected that some people may experience feelings of claustrophobia or anxiousness from wearing a mask.

  It is expected that some people may experience increased pressure around the area of the mask, this is expected to be temporary and resolve once mask is removed.

  Subjects should not take part in this study if they are allergic to adhesives. Subjects' answers on the health questionnaire will help the medical staff decide if they can safely participate in this study; subjects are encouraged to let the study staff know if they have any concerns.

- **Risks Associated with Shaving**

  Subjects may be asked to shave the area of sensor and/or mask application to allow the sensors and/or mask to adhere to the skin. Risks associated with shaving include cuts and/or abrasions, bleeding, infection, razor burn, rash, itching skin, flushing or redness of the skin, unusually warm skin, skin inflammation, skin irritation, ingrown hairs, and/or inflamed hair follicles. Each of these discomforts and side effects are temporary and should fade over time. Some of these symptoms may last up to several days after shaving.

  If there are any cuts and/or abrasions near the area of sensor and/or mask application, certain types of sensors or masks may not be placed on the particular location to avoid any discomfort for the subject.

  Within the consent form, subjects will agree to have sensor adhesion sites shaved or not. Subjects can stop these measures at any time if they feel uncomfortable.

- **Risk from Carbon Dioxide Administration:**

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

  Other anticipated adverse events that may occur, include but are not limited to: tingling, prickling sensations ("pins and needles" feeling), restlessness, sudden increase in blood pressure/sudden drop in blood pressure, sudden increase in heart rate/sudden drop in heart rate, irregular heart rate (PAC, PVC, EKG abnormalities, etc.), sweating, and/or feeling

claustrophobic or anxiousness from wearing a mouthpiece and/or mask.

These anticipated adverse events are expected to be temporary.

- **Low Oxygen Concentration Risks:**

  Risks associated with hypoxia include dizziness, shortness of breath, drowsiness, and/or headache. If or when this occurs, 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.

  Other anticipated adverse events that may occur, include but are not limited to: vasovagal syncope (fainting), lightheadedness, chest discomfort (e.g. chest tightness, chest pain), feeling flush/warm, feeling of anxiety, feeling nauseated, throwing up, seizures, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, irregular heart rate (PAC, PVC, EKG abnormalities, etc.), tingling sensation of face, arms and/or legs, sweating, mouth dryness, feeling claustrophobic or anxiousness from wearing a mouthpiece and/or mask. These anticipated adverse events are expected to be temporary.

[redacted]

- **Lidocaine (injection) Risks:**

  Injection of the Lidocaine may be discomforting and can feel like a slight pinch along with a warm/burning sensation.

  Other anticipated adverse events that may occur, include but are not limited to: 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/or tremors.

  Although not common, it is also possible to have an allergic reaction to injectable lidocaine (e.g., seizures). 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 hives; difficulty breathing; swelling of the face, lips, tongue, or throat.

  These adverse events are expected to be temporary.

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

  Ethyl Chloride and Pain Ease are topical anesthetics used to prevent pain by cooling the skin.

  Although unlikely, the anticipated adverse events that may occur, 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. These adverse events are expected to be temporary.

- **Risks Associated with Motion**

  This study may include manual motion or motion by means of a motion generator. The subject may be requested to tap their fingers, make a rubbing motion, tapping motion, waving motion, etc.

  Although unlikely, the anticipated adverse events that may occur, include but are not limited to: muscle fatigue, muscle/tendon strain, bruising from tapping a hard surface, temporary changes in heart rate, and/or temporary changes in breathing rate.

These adverse events are expected to be temporary.

- **Risk from Inflicted Knowledge:**

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

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

- **Risk from Loss of Confidentiality:**

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

- **Risk from Additional Testing:**

  During the conduct of the study, it is possible, but not likely, that someone could become exposed to a sample of blood drawn from the subject through an inadvertent needle stick or by contact with an open cut. In such circumstances, it will be important to the exposed individual to know whether the blood to which he or she was exposed contained Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), or Human Immunodeficiency Virus (HIV).

  In the case that an individual becomes exposed to a sample of blood from the subject, the subject will be requested to go to an outside facility (e.g., urgent care clinic, outside laboratory) and have an additional sample(s) taken for additional testing. The test results will be maintained as confidential and will only be used by healthcare professionals for the diagnosis and treatment of the exposed individual as appropriate.

  In the case that Masimo needs to contact a subject regarding additional testing, they will be contacted by a Masimo employee and medical personnel can be available for further counsel if requested.

  The cost for the initial testing and compensation for their time/travel to the testing facility will be the only things paid for by Masimo.

4.3. Measures Taken to Protect the Rights and Welfare of Subjects

All subjects will be monitored closely throughout the study. There will be an ACLS certified medical doctor present in the study area throughout the study.

The following measures will be taken to ensure the confidentiality of the subjects:

- A code (identification) number for each subject will be kept on file.
- Only their corresponding identification number will identify subjects.
- Access to identifying documents and data will only be made to the principal investigators in the study and study staff.
- The confidentiality and retention of these documents will be protected to the extent provided and required by the law.

4.4. Emergency Response Plan for Medical Emergencies

The physician and nurse present during the study will be ACLS certified and will respond to any medical emergency involving a subject with the ACLS approved protocol for intervention. A crash cart equipped with medications to provide immediate care during emergencies is on site and full emergency services are within 3 miles.

4.5. Alternatives

The alternative is to not participate in the study.

5. OBJECTIVES OF THE CLINICAL INVESTIGATION

The primary objective of this study is to:

- Validate performance of the Masimo INVSENSOR00040 functional arterial oxygen saturation (SpO2) on a diverse subject population during no motion conditions across an arterial saturation (SaO2) range of 70-100%, against reference arterial blood samples analyzed by a laboratory CO-oximeter reference instrument for SpO2
- Validate performance of the Masimo INVSENSOR00040 Pulse rate (PR) within its specified range on a diverse subject population during no motion conditions while undergoing desaturations protocols, against reference Standard of care EKG monitor measuring HR.

Data using the noninvasive devices will be collected from generally healthy male and female volunteers undergoing a desaturation procedure. Study subjects of differing levels of skin pigmentation will be enrolled in the study.

This is a nonrandomized single arm study wherein all subjects are enrolled into the experimental arm and receive the INVSENSOR00040 on one wrist. Desaturation will be conducted by reducing the concentration of oxygen the study subject breathes in a controlled manner to obtain noninvasive oxygen saturation readings, SpO2, at various levels. Reference blood samples will be repeatedly collected from the subject and analyzed using a standard laboratory CO-oximeter.

SpO2 performance will be calculated using Accuracy root mean square (ARMS) analysis of the SpO2 values and the reference CO-oximeter values.

PR performance will be calculated using Accuracy root mean square (ARMS) analysis of the PR values and the reference EKG monitor HR values.

Outcome Measure:

- SpO2 Performance will be determined by calculating the ARMS value through the comparison of the noninvasive oxygen saturation measurement (SpO2) to the arterial oxygen saturation (SaO2) value obtained from a reference blood sample.
- PR Performance will be determined by calculating the ARMS value through the comparison of the PR to the HR values from a reference standard of care EKG monitor.
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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 INVSENSOR00040 on one wrist. Desaturation will be conducted by reducing the concentration of oxygen the study subject breathes in a controlled manner to obtain noninvasive oxygen saturation readings of SpO2, at various levels, PR and RR.

- Reference blood samples will be repeatedly collected from the subject and analyzed using a standard laboratory CO-oximeter. The performance will be calculated using Accuracy root mean square (ARMS) analysis of the SpO2 values and the reference SaO2 values from a CO-oximeter.
- PR Performance will be determined by calculating the ARMS value through the comparison of the PR to the HR values from a reference standard of care EKG monitor.

[redacted]

6.1.2. Measures Taken to Minimize/Avoid Bias:

Subjects are selected from the population surrounding the clinical research site. Where applicable, subjects with required demographics (e.g., skin tone, gender, etc.) may be preferentially recruited.

6.1.3. Equipment and Materials

Equipment and Materials: All lab analyzers and equipment will be maintained per manufacturer specifications and all study personnel will be trained on the use of relevant equipment. Equivalent equipment and materials to those listed below may be used.

Safety Equipment (FDA-Cleared)

- Blood pressure monitoring system [redacted]
- Electrocardiogram (ECG)
- Masimo Pulse Oximeters (Radical-7)
- Masimo Patient Monitoring Platform (Root®) with accessory OR+ Multigas Monitoring.
- Pulse oximeter sensors and cables (Masimo SET, Masimo rainbow, or comparable)
- Medical-grade oxygen tank, mask, and nasal cannula
- Crash cart

Test Devices

- Masimo INVSENSOR00040 – investigational

Research Equipment

- Optional: Masimo INVSENSOR00039 - investigational [redacted]
- Colorimeter (e.g., Delfin SkinColorCatch)
- Motion Generator: a device designed to uniformly move a person's arm at a given frequency and amplitude. [redacted]
- Laboratory co-oximeters/blood analyzers

6.1.4. Completion of the Clinical Investigation

The clinical investigation is considered complete when adequate data has been collected as per the sampling plan.

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

The investigational INVSENSOR00040 used in this study is similar to commercially available wearable health monitoring devices except that it has a continuous SpO2 function. The investigational INVSENSOR00040 does not pose any additional risk to patients.

Masimo INVSENSOR00039 and/or other FDA-cleared or other commercially available pulse oximeters may be used for research purposes.

6.3. Subjects

6.3.1. Eligibility Criteria

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

Inclusion Criteria (Eligible Subjects)

- Subject is 18 to 50 years of age.
- Subject weighs a minimum of 110 lbs.
- Subject has a hemoglobin value ≥ 11 g/dL.
- Subject's baseline heart rate is ≥ 45 bpm and ≤ 85 bpm.
- Subject's CO value is ≤ 3.0% FCOHb.
- Subject's 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.
- Subject is able to read and communicate in English and understands the study and the risks involved.

Exclusion Criteria (Ineligible Subjects) (* = Per Physician Discretion)

- Subject whose skin is not intact and/or has tattoos in the area of device placement (e.g., wrist).*
- Subject is pregnant.
- 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 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 Wolff-Parkinson-White Syndrome or Stokes-Adams Syndrome.
- Subject has any symptomatic 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 active signs and/or symptoms of infectious disease (e.g. hepatitis, HIV, tuberculosis, flu, malaria, measles, etc.).*
- 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, or uncontrolled hypertension.
- Subject has delivered vaginally, has had a pregnancy terminated, 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 (working out, riding a bike, riding a skateboard, etc.), or any activity that will put additional stress on the wrist within 24 hours following a study that involves an arterial line.
- 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.

6.3.2. Expected Duration of the Clinical Investigation and Subject Participation

Expected duration of study enrollment is 3 to 6 months. Subject participation in the study will be approximately 180 minutes.

6.3.3. 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.

6.3.4. Replacement of Subjects

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

6.3.5. 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 in order 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.

6.4. Procedures

6.4.1. Schedule of Activities

6.4.2. Recruitment and Prescreening

6.4.3. Consenting and Screening

Subjects must read and sign the IRB-approved informed consent document. No study related activities will be conducted until the consent form is signed.

After informed consent is obtained, subjects will be asked a brief series of health questions to ensure their eligibility for this study. Subjects who do not meet the inclusion criteria and/or meet exclusion criteria will not be eligible to participate in the study.

[redacted]

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

In addition, a medical history will be recorded after the initial screening questionnaire. [redacted]

An orthostatic blood pressure test is ONLY required to be performed on subjects that meet the following criteria:

[redacted]

The following combinations meet the criteria for performing an orthostatic blood pressure measurement. If the criteria are not met, an orthostatic blood pressure test is not required.

[redacted]

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

The orthostatic blood pressure test will start with the clinician taking the subject's blood pressure while they are lying in supine position. The subject will then stand up for 30 seconds and a second blood pressure measurement will be taken. The subject's blood pressure will need to stay above [redacted] to meet inclusion criteria for the study.

Female subjects will be required to take a pregnancy test. Results will be noted in study documentation. If the pregnancy test is positive, the subject will be notified and removed from the study.

[redacted]

6.4.4. Procedure

The subject will be seated and/or lying-in supine position and should refrain from excessive movement during the study.

If accepted into the study, the subject's vitals will be monitored with standard noninvasive monitors, including FDA-cleared pulse oximeters, ECG, and blood pressure cuff. Information from these monitors may optionally be recorded.

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.

[redacted]

[redacted]

Local anesthetics such as lidocaine or skin refrigerant (e.g. Ethyl Chloride or Pain Ease) may be used if 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.

[redacted]

[redacted], the study device(s) will be placed on the subject's wrist. Data collection will be initiated using the automated data collection software. Sensors may be repositioned, as needed, to ensure proper placement. When the INVSENSOR00040 is placed for an extended period of time, the site should be assessed as frequently as every 1 hour. If there are any signs of loss of skin integrity and/or loss of circulation or perfusion, the device should be repositioned. The device must be removed prior to defibrillation.

Pulse oximeter output values (e.g., SpO2, pulse rate) will be recorded using the data collection software. Raw absorbance data from the noninvasive device(s) will also be recorded using the data collection software.

Upon successful placement of the sensors and the subject's indication that they are comfortable, a baseline set of blood samples will be obtained.

A qualified person will complete blood draws. [redacted]

Upon indication that the subject is comfortable, a gas mixture will be administered through the mouthpiece. The gas mixture may include varying proportions of oxygen, carbon dioxide, and nitrogen. The proportion of oxygen in this mixture will be decreased in a controlled manner to lower the subject's blood oxygen saturation. The lowest targeted value will be 70% oxygen saturation. Readings near 70% will be immediately verified by the reference CO-oximeter to ensure that levels are within the targeted oxygen saturation range and to minimize time that the subject may drop below the targeted range. At any point in the study, if the subject feels uncomfortable, the subject will be given oxygen.

[redacted]

The timing of the blood samples will be entered into the data collection software. To allow for pulse oximeter instrument response times, the subject should be at the desired saturation level for approximately 30 seconds before and after a blood sample is taken.

The study will end at a FiO2 equal to or greater than room air (>21%) to help the subject re-saturate after the procedures. If at any point the subject is uncomfortable with the study, the study will be stopped.

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

During the study, subjects may be recorded using photography and/or videography. The recordings may include sound. These

recordings may capture identifying features on the hand and/or arm. These recordings may be used in research, product development, product testing, training, and comparison study purposes. Subjects will be given the option to provide consent or opt-out of the recordings

6.4.5. Ending Procedure

Study staff may take [redacted] to verify the subject's blood values are within normal ranges (e.g., pH, glucose, etc.).

The total overall lab time will be approximately [redacted]. In the event that the total lab time exceeds [redacted], subjects will be compensated for the extra time. Subjects will be paid according to the compensation breakdown on the consent form.

At the conclusion of the procedure, the sensor(s)/device(s), IV(s), and [redacted] 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. Subjects will be given instructions on post care. All subjects will be instructed to contact the principal investigator or study staff in the event of any potential complication.

Subjects will be offered a snack and water or juice. Subjects are asked to consume food and/or liquid prior to leaving the clinical lab area for their safety due to study procedures such as blood removal and [redacted]. Subjects may also be asked to wait in the clinical lab or lobby waiting area for up to an additional 30 minutes before leaving to allow for their body to continue adjusting after the study has completed.

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]

The subject will be allowed to leave after medical personnel determine it is safe to do so.

6.5. Monitoring plan

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

7. STATISTICAL DESIGN AND ANALYSIS

7.1. Acceptance Criteria

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

7.2. Sample Size

a. Per ISO-80601, validation studies should enroll, at a minimum, at least 10 subjects and collect 200 samples across all subjects. In typical desaturation studies, the number of samples for each subject will vary depending on the subject's ability to reach and maintain the targeted SaO2 level. [redacted]

b. The final analysis will utilize statistical methods to ensure accuracy statistics are calculated with comparable density over the range 70-100 % SaO2 and adjust for repeated measures within subjects.

c. 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. Exclusion

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;

iii. Reference device malfunctions and/or provides inconsistent values;

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

v. Low signal quality, e.g. due to noise or interference.

vi. Subject's oxygen saturation is unstable. This is determined using multiple consecutive blood draws, to be stable within 1% SaO2 (as obtained from a reference device) to include the measurement pair.

b. Accuracy calculations

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

$$Bias = \frac{1}{n}\sum_{i=1}^{n}(SpO2 - SaO2)$$

$$\text{Precision} = \sqrt{\frac{\sum_{i=1}^{n}((SpO2 - SaO2) - Bias)^2}{n}}$$

$$A_{RMS} = \sqrt{\frac{\sum_{i=1}^{n}(SpO2 - SaO2)^2}{n}}$$

The A_{RMS} and precision values 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 screen failure, they are unable to complete desaturation criteria, or they are unable to have intravenous or arterial line placed. Expected drop out rate for this study is approximately 50% of the subjects who consented to participation in this 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 study 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

Subjects must read and sign the consent document using the informed consent process as outlined in FRM-3451 Informed Consent Process. No study-related activities will take place prior to informed consent.

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

14.1. Definitions

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

- adverse event: untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated (ISO 14155)
- adverse device effect: adverse event related to the use of an investigational medical device
- serious adverse event: adverse event that led to any of the following:
    - a) death

- b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
  - 1) a life-threatening illness or injury, or
  - 2) a permanent impairment of a body structure or a body function including chronic diseases, or
  - 3) in-patient or prolonged hospitalization, or
  - 4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,
- c) fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment

Note: Planned hospitalization for a pre-existing condition, or a procedure required by the Clinical Investigation Plan, without serious deterioration in health, is not considered a serious adverse event.

- serious health threat: signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons.

  Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

- serious adverse device effect: adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

- unanticipated serious adverse device effect: serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment

  Note: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

- device deficiency: inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance

Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling.

Note 2: This definition includes device deficiencies related to the investigational medical device or the comparator.

14.2. List of non-reportable adverse events

All adverse events will be reported to Sponsor.

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. Vulnerable population

14.5. 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.

14.6. Protection of vulnerable subjects

- Employees may be enrolled into this study. Participation is not a condition of employment. There will be no repercussions in the workplace in the case that the employee refuses to participate in the study or withdraws at any point during the study. Neither supervisors nor superiors will be involved in the recruitment of employees for participation in the study.
- 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.

14.7. Responsible Parties

- The IRB will review research with vulnerable populations and evaluate consent, level of risk, coercion, and the reason for choosing this particular subject population. The IRB will be responsible for determining what practices will include continuing review for compliance while monitoring these studies.
- The Investigator holds the ultimate responsibility for protecting the rights, safety, and welfare of research subjects by ensuring that all regulations and proper documentation of consent is handled in a compliant and timely manner.

15. SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

15.1. 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 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 along with 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.

15.2. 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.

16. 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 publically available.

17. BIBLIOGRAPHY

ISO-80601-2-61:2011 Medical electrical equipment -- Particular requirements for the basic safety and essential performance of pulse oximeter equipment for medical use

18. REVISION HISTORY
