Official Title: Oxygen Reserve Index Validation for RD Lite Sensors

Date of Protocol: August 1, 2017

NCT Number: NCT03128892

Protocol/Test Procedure Title	Oxygen Reserve Index (ORI)
Lead Investigator	Tala Harake, MS, BS Clinical Lab Manager Masimo Corporation 52 Discovery, Irvine, CA 92618
Other Investigators	[redacted] Assistant Clinical lab Manager Masimo Corporation 52 Discovery, Irvine, CA 92618 [redacted] Clinical Research Associate Masimo Corporation 52 Discovery, Irvine, CA 92618
Expected Start Date	Based on IRB Approval Certification Approval Date
Expected End Date	Based on IRB Approval Certification Expiration Date
IRB	E&I West Coast Board – IRB00007807
Date Submitted To IRB	

Protocol Test Abstract:

This document describes a procedure to collect optical and invasive reference data for the development of Masimo's devices and sensors. Non-invasive data from devices and blood levels of oxygen reserve index (ORI) as well as other non-infectious blood solutes will be measured during [redacted] conditions in order to evaluate and calibrate the system. This protocol may involve optical data collection, placement of arterial and venous line(s), and intermittent blood sampling for reference machines.

APPROVALS

Author	Date	Engineering	Date
Quality Assurance	**Date**	**Manufacturing**	**Date**

This document is a protocol for a clinical research study sponsored by Masimo Corporation. The study will be conducted in compliance with all stipulations of this protocol, the conditions of IRB approval, the Declaration of Helsinki, ISO-14155, applicable regulatory requirements and International Conference on Harmonization Good Clinical Practice guidelines ICH GCP.

1. PURPOSE

The primary objective of this study is to collect data using noninvasive devices from healthy volunteers undergoing a desaturation procedure. [redacted]

Devices to be used in this study will use Masimo SET technology and Masimo Rainbow technology sensors. Devices and sensors may be FDA-cleared or investigational. [redacted]

All investigational devices and sensors undergo a risk assessment evaluation prior to use on human subjects to safeguard subjects. No device or sensor that fall under a significant risk device classification as defined in 21 CFR 812.3(m) and determined by the IRB will be used under this protocol.

[redacted]. Pulse oximeters or similar non-invasive devices that are FDA approved or that are investigational may also be tested during this study if needed.

[redacted]

[redacted]

2. BACKGROUND

Masimo Corporation develops non-invasive medical technologies. These devices have applications in the operating room, critical care unit, emergency room, emergency transport vehicles, as well as physician's offices.

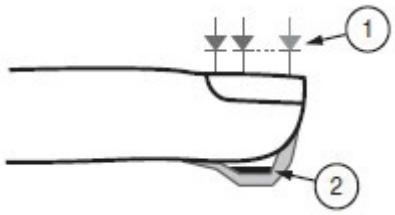
A blood sample gives the best measure of hemoglobin as well as other blood solutes but is difficult to measure continuously and without skin puncture and risk of infection. Masimo SET and Masimo Rainbow technology allows real-time, non-invasive monitoring of hemoglobin (and other blood

solutes) in patients and has the potential to improve clinical outcomes while reducing the cost of care and risks to both patients and clinicians associated with venipuncture.

2.1 TECHNOLOGY BACKGROUND

Pulse oximetry is governed by the following principles:

1. Oxyhemoglobin (oxygenated blood) and deoxyhemoglobin (non-oxygenated blood) differ in their absorption of red and infrared light (spectrophotometry).
2. The amount of arterial blood in tissue changes with arterial pulses (photoplethysmography). Therefore, the amount of light absorbed by the varying quantities of arterial blood changes as well.
3. More generally, Masimo Pulse CO-Oximeters use a multi-wavelength sensor to distinguish between not only oxygenated blood and deoxygenated blood, but also blood with carbon monoxide, oxidized blood and blood plasma. The CO-Oximeter utilizes a sensor with various light-emitting diodes (LEDs) that pass light through the site to a photodiode (detector). See figure below.



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

4. Signal data is obtained by passing various visible and infrared lights through a capillary bed (for example, a fingertip, a hand, a foot) and measuring changes in light absorption during the blood pulsatile cycle. [redacted] The detector receives the light, converts it into an electronic signal and sends it to the Rad-57, or similar Masimo hardware platform, for calculation.
5. Once the oximeter receives the signal from the sensor, it utilizes Masimo SET signal extraction technology for calculation of the patient's functional oxygen saturation and pulse rate, total hemoglobin, and/or other physiological parameters.

2.2 STUDY DEVICES

Devices used in this study may be either:

- Masimo FDA cleared devices used according to the FDA-approved indication, or
- Masimo investigational devices, which:
  - Are FDA-cleared devices used outside the FDA approved indication, or
  - Are novel prototypes or modified versions of the FDA-cleared products (with or without minor hardware and software adjustments) that do not pose increased risks to subjects.
  - Are non-significant risk devices.
  - Undergo a risk assessment evaluation prior to use in human subjects to safeguard subject safety.

[redacted]

2.2.1 Current Masimo Predicate Devices

Masimo rainbow SET® is a noninvasive monitoring platform featuring Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry with the option to measure multiple additional blood constituents and physiologic parameters. Masimo rainbow and SET technology describes a line of sensors that all use the same pulse oximetry type technological concepts to read physiological parameters. Conventional pulse oximetry uses two LED (light emitting diodes) to emit light through one side of the finger and a detector on the other side that reads the amount of light that makes it through the digit. With rainbow technology Masimo uses additional wavelength LEDs in order to calculate more complex blood solute concentrations like hemoglobin concentration. The same principles described above that govern Masimo SET technology (pulse oximetry) also govern Masimo Rainbow technology. These additional LEDs do not present any additional risk to the end user since they radiate light in the same wavelength and power ranges.

Depending on the number and type of LED Emitters, the investigational device can provide non-invasive estimates of a number of physiological parameters. See Table 1.

Oxygen Saturation (SpO2)	Pleth Variability Index (PVI®)
Pulse Rate (PR)	Methemoglobin (SpMet®)
Perfusion Index (PI)	Carboxyhemoglobin (SpCO®)
Total Hemoglobin (SpHb®)	Acoustic Respiration Rate (RRa®)*
Oxygen Content (SpOC™)	[redacted]

Table 1. ***List of currently FDA cleared Masimo non-invasive technology.***

2.2.2 Masimo Rainbow Pulse CO-Oximeter and Other Non-Invasive Sensors

The Masimo Rainbow SET CO-Oximeter platform is FDA 510(k) cleared for the noninvasive and continuous monitoring of total hemoglobin concentration in adults. The devices under test may be investigational versions of the Masimo [redacted] approved pulse oximeters, sensors or other monitoring devices.

Investigational devices are modifications of FDA-cleared products. They may differ from FDA-cleared products [redacted] Each aspect of the investigational device's modification is considered for impact on subject safety, and all investigational devices undergo a risk analysis assessment to identify required safety tests or risk mitigation strategies prior to use on any study subject. [redacted]

[redacted]

3. REFERENCE

Below is a full list of documents relevant to this protocol and study conduct under this protocol. Please reference this list if additional information is needed on any specifics of this study.

Documents Related To This Study:

- Consent to Act as Human Research Subject
- Subject Gender & Ethnicity Questionnaire
- Post Care Instructions
- Oxygen Reserve Index (ORI) Case Report Form (CRF)
- Oxygen Reserve Index (ORI) Advertisement
- Oxygen Reserve Index (ORI) Recruitment Script
- Oxygen Reserve Index (ORI) Health Questionnaire
- - Confidentiality Agreement
- W-9 Request for Taxpayer Identification Number and Certification
- Volunteer payment form

Administrative Documents:

- Informed Consent Process
- Device Accountability Log

Regulations/ Guidance:

- Desaturation Test System Calibration Procedure
- Radical 7 Operator's Manual
- 21 CFR Part 812 Investigational Device Exemptions
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 56 - Institutional Review Board
- 21 CFR Part 54 – Financial Disclosure by Clinical Investigators
- Council Directive 93/42/EEC of 14 June 1993 concerning medical devices
- The Declaration of Helsinki
- ISO 14155:2011 Clinical investigation of medical devices for human subjects – Good clinical practice
- MEDDEV 2.7.1, December 2009: Evaluation of Clinical Data: A Guide for Manufacturers and Notified Bodies
- The Belmont Report
- 21 CFR Part 11 – Electronic Records and Electronic Signatures
- 21 CFR Part 50 – Protection of Human Subjects
- 21 CFR Part 801 – Labeling
- 45 CFR Part 46 – Protection of Human Subjects
- Guidance for Adverse Event Reporting to IRB's
- ICH Clinical Safety Data Management
- ICH Guidelines for Good Clinical Practice
- The Nuremburg Code
- Title 24 Chapter 9 360c – Classification of Devices Intended for Human Use

[redacted]Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard – Sixth Edition (H3-A6, Vol. 27 No. 26)
[redacted]Arterial Blood Gas Sampling
[redacted]Body Mass Index Table

4. LOCATION

Masimo Corporation
52 Discovery
Irvine, CA 92618

(Any other locations will be added by modification)

5. EQUIPMENT, MATERIALS AND SAMPLE SIZE JUSTIFICATION

5.1. Safety equipment and Blood Analyzers Maintenance:

5.1.1. All blood analyzers, ECG monitors, Blood pressure monitors and safety equipment will be maintained per manufacturer specifications and all study personnel will be trained on the use of relevant equipment.

5.1.2. The blood pressure cuff, ECG monitors, and FDA cleared oximeter will be used for monitoring of the participants for their safety.

5.1.3. The blood analyzers will be used to run blood samples collected throughout these studies for analyzing blood solutes that are relevant to specific noninvasive technology readings being tested. e.g. Blood will be run for purposes of reading hemoglobin from sample compared to non-invasive hemoglobin reading from Masimo Hemoglobin sensor.

5.2. Equipment and Materials: to be used as required [redacted] Standard safety monitors will be used for this study (e.g. ECG, FDA-cleared pulse oximeter, BP cuff)

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

Subject safety monitoring equipment and medical supplies

- Non-invasive blood pressure arm cuff(s)
- ECG monitor – FDA approved product
- Urine HCG pregnancy test -female subjects only
- Standard band aids, needles, syringes, sharps container or other standard medical, wound care equipment and biohazard waste containers necessary to carry out the test procedure
- Standard Emergency equipment and medications will be available in on-site during the study
- 0.5%-2% lidocaine
- Ethyl Chloride/Pain Ease
- Heparin or saline flush solution (as required)- or equivalent
- Arterial blood pressure transducer

FDA-Cleared devices and sensors

- Rainbow Sensors
- Conventional Pulse Oximeters
- Conventional Pulse Oximeter Sensors

Investigational devices and sensors

- Pulse Oximeters
- Pulse Oximeter Sensors
- Pulse Oximeter Patient Cables

Oxygen administration equipment

- Medical grade O_2
- Oxygen mask
- Mouthpiece
- Nasal Cannula

Desaturation equipment and safety equipment

- Gas tanks, regulators

General lab supplies

- Stopwatch

5.3. Sample size justification

5.4. Standard Precautions

5.4.1. Subjects will have continuous ECG monitoring throughout the study (may not be recorded/ for monitoring by medical staff).

5.4.2. ACLS certified physician will be in attendance (in the study space) throughout the entire procedure, and the study will be completed under their general supervision.

5.4.3. Any emergency drug deliveries in the case that a subject loses consciousness or has another emergency arise (standard crash cart medications- atropine, ephedrine etc.) shall be recorded. This individual will be monitored and this information will be recorded and submitted to the IRB if necessary (unanticipated adverse event) and the subject will be given the option to follow up with a local urgent care facility.

5.4.4. The volunteer will be monitored (through observation by clinical study staff) throughout the study procedure.

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

5.4.5. All adverse events will be recorded.

6. PROCEDURE

Overview: During this study we will recruit human subjects; this will include members of the general public and Masimo employees, to participate in a study. During this study we will be testing the sensors in order to make a desaturation assessment of our noninvasive devices (listed above). Participants in this study will come in and be seated, review the consent information, agree or not. One or more clinician(s) will place and arterial line(s), and sensors will be placed. The clinician will collect blood samples which will be run on our internal blood analysis equipment (.). This blood sampling will serve the purposes of a comparison tool for the readings that were recorded from the noninvasive devices and sensors.

Pulse oximetry monitoring will take place throughout the study. During this study subjects : continuous reference blood sampling and oxygen administration.

6.1 RECRUITMENT

6.1.1 Advertisement

Recruitment materials are posted publically in local newspapers, Craigslist, schools/universities etc.

6.1.2 Phone Screening

Potential subjects can contact Masimo to inquire more details about the study. The recruitment process is managed by the designated person(s) who is trained for phone screening/scheduling. Appointments are made once the phone screening process is completed and the person screening the subject determines if they qualify or not for the study based on inclusion and exclusion criteria.

[redacted]

6.2 PRE-ENROLLMENT SCREENING AND EXAM

6.2.1 Subjects will be asked to provide a copy of their valid government photo ID and/or Social Security (SSN) to verify subject information in our scheduling database and/or to verify the subjects' identity. Foreign persons (A foreign person includes a nonresident alien individual and certain foreign entities that are not U.S. persons) will 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).

The copies of these forms of identification will be stored along with the subjects consent documents. The confidentiality and retention of these documents will be protected to the extent provided and required by the law.

The SSN number and ID card is kept to verify subject's identities or instances to track subjects who provide false identification.

6.2.2 Subjects will be informed of the procedure prior to participating in the study. Subjects must read and sign the consent document, using our informed consent process. The consent form must be stamped with a current IRB approval. No study related activities will be conducted until consent is signed.

6.2.3 Weight is self-reported by the subject, but if the subject appears to be outside the weight range based on the inclusion/exclusion criteria, subjects will be weighed on a scale.

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

6.2.5 Subject demographic information including age, sex, skin tone, ethnicity, height and weight will be collected.

6.2.6 In addition, a medical history will be recorded after initial screening questionnaire. Pre-procedural vital signs will be recorded for subject safety monitoring.

6.2.7 Female subjects 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.

6.2.8 A venous blood sample will be obtained and analyzed [redacted]

6.2.9 Blood samples will be discarded after testing. These samples will be discarded in the appropriate biohazard waste bins and the samples are de-identified

6.2.10 Subjects may have a blanket placed on them (per request of subject or staff).

6.2.11 Subjects may be offered a snack (ie. Granola bar) and/or beverage (ie. Water, juice) due to the amount of time their involvement in this study may take.

6.3 PRE DESATURATION PROCEDURE

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

6.3.2 Safety monitors will be placed on the subject, which may include FDA-cleared pulse oximetry, ECG, and blood pressure (may not be recorded automatically depending on the protocol, this may be recorded manually by medical staff).

6.3.2.1 Post Qualification: Spikes in blood pressure and heart rate can be expected during (but is not limited to) 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 continuation of the screening procedure. 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. This will be left to the discretion of medical and study staff.

[redacted]

6.3.5 Upon successful placement of the , Arterial line and the volunteers' indication that they are comfortable, optical sensors for noninvasive measurement(s) will be placed on the subjects fingers.

6.4 ORI PROCEDURE

6.4.1 Upon successful placement of the safety monitors and the volunteer's indication that they are comfortable, a baseline set of blood samples will be obtained.
A qualified person will complete blood draws.

6.4.5 Subjects will be given supplemental oxygen through a nasal cannula, mouth piece or mask during some portion of the study. This is to simulate the high oxygen environments and test our sensors performance during oxygen administration.

6.4.7 The process will be stopped if there is any evidence of volunteer stress or distress.

6.4.9 Any blood not used for analysis will be discarded.

[redacted]

6.4.11 Other standard output parameters may also be recorded from the device(s) (SpO2, SpMet, SpCO, PVI, PI, pulse rate are some examples of these).

6.5 DESATURATION PROCEDURE

[redacted] Subjects may also be taken to different saturation levels below room air. [redacted]

6.5.2 Note: There will be a medical grade oxygen tank next to the subject, equipped with an oxygen mask, ready for a scenario where a subject needs 100% oxygen immediately. At any point in the study, if the subject feels uncomfortable, the subject will be given 100% oxygen. The subject's mouthpiece and nose clip will be removed and oxygen will be administered until medical personnel determine the subject is asymptomatic and the subject acknowledges they are feeling better.

[redacted]

6.6 ENDING PROCEDURE

6.6.1 The total time will be approximately [redacted]

6.6.2 At the conclusion of the procedure, the sensors/devices [redacted] and the arterial line(s) will be removed and the volunteer will be allowed to leave after medical personnel determine it is safe to do so.

6.6.3 All volunteers 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. All subjects including subjects that are employees of Masimo will be advised to take as much time as they need after the study before returning to work.

6.6.4 Volunteers will be given instructions on wound care. All volunteers will be instructed to contact the principal investigator and/or study staff in the event of any potential complication.

6.6.5 Volunteers will be paid according to the compensation breakdown on the consent form.

6.6.6 Subjects will be provided with information related to any significant new findings that develop at any time during the study which may relate to their willingness to continue their participation, their health and/or medical care.

6.7 TIMING REQUIREMENTS FOR SUBJECT PARTICIPATION

[redacted]

[redacted]

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

7. ACCEPTANCE CRITERIA (IF APPLICABLE)

[redacted]

8. DATA ANALYSIS PROCEDURE TO BE USED

[redacted]

8.2. Sample size and level of significance and power

[redacted]

8.2.1. Study variables

8.2.1.1. Devices (see section 2 for descriptions and limits)

8.2.1.2. Procedures (see section 6 for descriptions and limits)

8.2.1.3. Subjects (see section 9 for descriptions and limits)

8.2.1.4. Other: None allowed unless named.

8.2.2. Measures taken to minimize/avoid bias:

8.2.2.1. Subjects are selected from the population surrounding the test site (including employees). Where applicable, subjects with required demographics (skin color, age, gender, etc.) may be preferentially recruited.

8.2.2.2. Sensors and devices will be provided to operators in a way that [redacted]

8.2.2.3. Operators will not make any decisions based on results from other operators or any parameters obtained from blood samples.

8.3. Statistical Design

[redacted]

8.3.2. When applicable, [redacted] describe any reasons for terminating the study early.

[redacted]

8.4. Data Quality Assurance

8.4.1. The investigator/study staff shall prepare and maintain accurate case histories designed to record all observations and other data pertinent to the study for each study participant. All information shall be recorded on the case report forms.

8.5. Case Report Forms

8.5.1. Data shall be entered into a Case Report Form. The relevant data on the Case Report Forms will be transferred into a database for analysis. No subject identifiers will be collected on the Case Report form. Access to the completed Case Report Forms will be locked and the Study Database will be password protected, both limited to study personnel.

8.5.2. Case report forms will capture protocol deviations and will prompt any notifications to the IRB.

8.6. Expected Dropout Rates

There are two possible dropout causes:

8.6.1. The first is if the sensor/device fails to provide a valid reading on a Subject. Depending on desired endpoints and parameter statistics, [redacted] may address how many valid measurements are required to include a subject in the analysis. The second is if the Subject does not wish to complete the study. All subjects have the right to terminate the study at any time. Depending on the number of valid measurements taken prior to termination, the sponsor may elect to keep the collected data.

[redacted]

9. SUBJECTS

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

Inclusion Criteria (Eligible Subjects)

- Competent non-smoking (smokers including e-cigarette users) adults between the ages of 18 and 50 years of age.
  - We may also be interested in specifically recruiting smokers for some portions of this study as well as non-smokers for other portions of this study.
- Must weigh a minimum of 110 lbs and no more than 250 lbs unless subject is over 6 feet tall.
- Must have a hemoglobin value greater than or equal to 11 g/dL.
- Baseline heart rate $\geq$ 45 bpm and $\leq$ 85 bpm.
- CO value $\leq$ 2.0% FCOHb (unless we are specifically interested in recruiting smokers)
- Physical status of ASA I or II (American Society of Anesthesiology Class 1; Healthy subjects without any systemic disease at all. American Society of Anesthesiology Class II; subjects with mild systemic disease)
  - The ASA definition strictly applies to the systemic disease portion of the classification
- Blood Pressure (Systolic BP$\leq$ 140 mmHg and Diastolic BP $\leq$ 90 mmHg).
- Able to read and communicate in English
- Has signed written informed consent
- Female, non-pregnant.
- Female subjects will be provided with a pregnancy test free of charge.

Exclusion Criteria (Ineligible subjects)

- Subjects who do not understand the study and the risks involved.
- Subjects with BMI > 35 that a medical professional classifies as morbid obesity or has an increased risk for participation
- Subjects with open wounds, lacerations, inflamed tattoos or piercings, visible healing wounds.
- Subjects with frequent or severe headaches and/or migraine headaches.
- Subject has known drug or alcohol abuse. Subjects who uses recreational drugs.
- Subject has experienced a head injury with loss of consciousness within the last year.
- Any chronic bleeding disorders (i.e. hemophilia)

- Any history of a stroke, myocardial infarction, seizures or heart attack.
- Any cancer or history of cancer (not including skin cancer).
- Chronic neurological diseases (i.e. multiple sclerosis, Huntington's Disease).
- Any cardiac dysrhythmias (i.e. atrial fibrillation)(without physicians clearance)
- Subject has known neurological and/or psychiatric disorder (i.e. schizophrenia, bipolar disorder) that interferes with the subjects' level of consciousness.
- Known or concurrent chronic usage of psychoactive or anticonvulsive drugs. Subjects with psychiatric conditions or are on psychiatric medications (i.e. tricyclic antidepressants, MAO inhibitors, Lithium, neuroleptics, anxiolytics or antipsychotics, except SSRIs).
- Subject has any medical condition which in the judgment of the investigator and/or medical staff, renders them ineligible for participation in this study, such as Reynauds Syndrome.
- Subject has Wolff-Parkinson-White Syndrome or Stokes-Adams Syndrome
- Inability to tolerate sitting still or maintain minimal movement for up to 90 minutes.
- For studies involving finger sensors: subjects with polished, gel or acrylic nails, skin abnormalities affecting the fingers or arms (such as psoriasis, eczema, angioma, scar tissue, burn, fungal infection), distinct finger edema, substantial skin breakdown damaged and/or finger nail deformities (specific finger will not be used, unless we are specifically testing sensors in use with nail polish, gel, and /or acrylic nails).
- Subjects who have/are currently taking anticoagulant medication.
- Subjects who have had caffeine consumption the day of the study.
- Subjects who have taken pain medication within 24 hours of start of study. Unless minimal preventative dose recommended for adults (discretion of physician).
- Subjects having either signs or history of peripheral ischemia.
- Subjects who have had invasive surgery within the past year- including but not limited to major dental surgery, gallbladder, heart, appendix, major fracture repairs (involving plates/ screws), jaw surgery, Urinary tract surgery, plastic surgery, major ENT surgery, joint replacement or gynecological surgeries, heart surgery or thoracic surgery.
- Subjects who have had minor surgery or conditions in the past two months including but not limited to minor foot surgery (bunion), arthroscopic procedure, blood donation, plasma donation, skin biopsy/ procedures, root canal, fractures, eye surgery, and other minor procedures.
- Subjects that have been on antibiotics had congestion, head colds, flu, ear infection, chest congestion will have a 2 week waiting period from the time of finishing medications and must have no more symptoms.
- Subjects with claustrophobia, or anxiety.
- Subjects who have been in severe car accidents or a similar type of accidents will have a 12 month waiting period, from the time of the accident; unless upon further medical history questions the physician determines it does not place the subject in any additional harm, increase their risk, or compromise the subjects' safety.
- Subjects who have had a concussion will have a 12 month waiting period, from the time of the concussion.
- Subjects with chronic unresolved asthma, lung disease or respiratory disease.
- Subjects with allergies to lidocaine, latex, adhesives, or plastic.
- Subjects with heart conditions, Diabetes or hypertension.
- Subjects who have given vaginal delivery will have a 6 month waiting period. Subjects who had a pregnancy terminated, a miscarriage or had a C-section will have a 12 month waiting period.

- Subjects who intend on participating in any heavy lifting, repetitive movement of their wrist (including riding a motorcycle) or exercise (working out, riding a bike, riding a skate board etc.), or any activity that will put additional stress on the wrist within 24 hours following a study involving an arterial blood draw and/or arterial line placement.
- Discretion of investigator/study staff

10. WITHDRAWAL OF SUBJECTS

Subjects must be withdrawn under the following circumstances:

10.1. The subject withdraws consent

10.2. Discretion of investigator/study staff

[redacted]

10.3. There is set criteria that will be used to determine if the subject qualifies to participate in this study. Based on the discretion of the investigator/study staff and/or the evaluation of the qualifying criteria they may be excluded from this study.

- If the investigator/study staff notices a trend with (not limited to these examples) the subjects' blood pressure fluctuating outside the parameters, their heart rate fluctuating outside the parameters, their need to repetitively void early and/or their inability to remain still for the majority of the study they will be removed from the study and may not be used as a participant in that particular study in the future. [redacted]

11. ADVERSE EVENTS

Definitions ([redacted]):

Adverse event: Any untoward medical occurrence in a subjects, users or other persons, whether or not related to the medical device under study.

Device-related adverse event: Adverse event related to, associated with, or caused by, the use of a medical device under study, including but not limited to events that may have been attributed to the device because of device failure or malfunction, improper or inadequate design, manufacture or user error.

Device deficiency: Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors and inadequate labeling.

- Device deficiencies will be reported according to department procedures.

Serious adverse event: Adverse event that: a) led to death, b) led to serious deterioration in the health of the subject, that resulted in: (i) a life-threatening illness or injury, (ii) a persistent or significant impairment of a body structure or a body function, (iii) in-patient or prolonged hospitalization, or (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or c) led to fetal distress, fetal death or a congenital abnormality or birth defect. NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.

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

11.1. Adverse Events

11.1.1 All adverse events that occur during the study shall be recorded on the Case Report Form even if the investigator/study staff assesses the adverse event as unlikely to be causally related to the test device or study procedures.

11.2. Serious Adverse Events

11.2.1 The investigator/study staff shall promptly report both serious adverse events and unanticipated adverse device effects to the sponsor within 48 hours. All serious adverse events will also be reported to the IRB per IRB reporting requirements.

11.2.2 At the time of discharge from the study, any unresolved serious adverse event(s) will be followed up by the investigator/study staff until the event(s) are resolved, stabilized or the patient is lost to follow-up or the adverse event is otherwise explained. The investigator/study staff will also instruct the subject to report any subsequent events occurring in the next 30 days, which the subject or the subject's physician believes might reasonably be regarded as caused by or have a reasonable possibility of being caused by the test device or procedures involved in the study.

12. MEASURES TAKEN TO PROTECT THE RIGHTS AND WELFARE OF SUBJECTS

12.1. 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.

12.2. The following measures will be taken to insure the confidentiality of the subjects:

12.2.1. A code (identification) number for each subject will be kept on file.

12.2.2. Only their corresponding identification number will identify subjects.

12.2.3. Access to identifying documents (IC, SSN, Photo ID) and data will only be made to the principal investigators in the study and study staff.

12.2.4. The confidentiality and retention of these documents will be protected to the extent provided and required by the law.

12.3. Documents and Database

[redacted]

12.3.1. Documents will be kept a minimum of 5 years after the specific product/tested for is no longer being made. If destroyed, these documents will be shredded and done by a certified company used for destroying medical and clinical data

[redacted]

12.4. Vulnerable Populations

12.4.1. Employees are considered to be a vulnerable population

12.4.1.1. 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.

12.4.1.2. Neither supervisors nor superiors will be involved in the recruitment of employees for participation in the study.

12.4.2. Economically disadvantaged or unemployed and educationally disadvantaged

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

12.4.2.2. Educationally disadvantaged subjects will be provided ample time to ask questions and comprehend information

13. RISKS/DISCOMFORTS

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

13.1. **Risks**

13.1.1. Risks can be categorized into the following categories:

- Those associated with the device
- [redacted]
- Those associated with placement of the arterial line (arterial cannulation)
- Those associated with blood draws
- Those associated with inflicted knowledge
- Those associated with the Lidocaine injection
- Those associated with the Lidocaine spray
- Those associated with low oxygen concentration
- Those associated with oxygen administration
- Those associated with the nose clip
- Those associated with loss of confidentiality/privacy
- Those associated with Additional testing

Note: In the very unlikely, worst case, complications from the study may result in death. The study shall be stopped by the subject or study staff long before this would occur.

13.1.2. Device Risk

13.1.2.1. 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.

13.1.2.2. There is an extremely small risk of damage to the subject's fingers, or other locations where sensors are placed, from the device including temporary skin irritation or discomfort associated with exposure to the sensor as well as potential temporary mechanical irritation or discomfort. There is a remote, yet possible, risk of a burn from the sensor. In the case of a sensor burn there is the potential for permanent skin damage (scar/discoloration).

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

[redacted]

13.1.4. Arterial Cannulation Risks:

13.1.4.1. The radial artery is the most common site for invasive blood pressure monitoring in anesthesia and critical care medicine because it is technically easy to cannulate and complications are uncommon, in part owing to the good collateral circulation of the hand. The widespread application of invasive

arterial pressure monitoring in anesthesia and intensive care is related to the extremely good safety record of this technique.

13.1.4.2. Other risks include bleeding, infection, hematoma, damage to the blood vessel and surrounding nerves, tendons or tissue; loss of feeling in hand and/or arm and even the loss of hand due to rare complications of the study.

13.1.5. Blood Draw Risks

13.1.5.1. Discomfort is generally associated with needle puncture. The most common complications associated with blood draws are hematomas or bruising.

13.1.5.2. There is also a possible risk of infection, tendon or tissue damage, damage to the blood vessel and surrounding nerves, loss of feeling in hand and/or arm and even the loss of hand due to rare complications of the study.

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

- Vasovagal (fainting)
- [redacted]
- Lightheadedness
- Feeling flush/ warm
- 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
- Mouth dryness

These anticipated adverse events are expected to be temporary.

The listed discomforts and complications associated with blood draws can be expected and are not an act of neglect, failure to follow standards or related to the sensors or devices used in the study.

13.1.6. Risk from Inflicted Knowledge

13.1.6.1. The risk of inflicted medical knowledge to volunteers is negligible since we de-identify all associated sample information including those relevant to our clinical and engineering parameter studies. The monitoring and test results are not examined for diagnostic purposes and do not reflect an attempt to ascertain any subject's medical condition. The attending physician's role during this study is to ensure the safety of the subject during the study. We will reduce the risk of inflicted knowledge by assuring the subjects that device readings and blood measurements are for research use only. In the case that a subject becomes aware of a condition (anemia, hypertension, arrhythmia etc.) they have during the course of our study our study staff will recommend that they contact their primary care physician and we will document this recommendation. As part of that process we will follow up with these individuals prior to enrollment if their condition meets exclusion for that particular study.

13.1.7. Lidocaine (injection) risks

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

13.1.7.2. 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

These adverse events are expected to be temporary.

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 called 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 your face, lips, tongue or throat.

13.1.8. Ethyl Chloride (Lidocaine Spray)

13.1.8.1. Ethyl Chloride is a topical anesthetic which is used to prevent pain by cooling the skin.

13.1.8.2. Although unlikely, the anticipated adverse events that may occur, include but are not limited to:

13.1.8.2.1. Changes in skin color (ie. Flushing or redness of the skin)

13.1.8.2.2. Delayed wound healing

13.1.8.2.3. Rash

13.1.8.2.4. Itching

13.1.8.2.5. Swelling

These adverse events are expected to be temporary.

13.1.9. Low Oxygen Concentration

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

13.1.9.2. 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.

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

- Vaso vagal (passing out)
- Lightheadedness
- 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
- Mouth dryness

13.1.9.3.1. These anticipated adverse events are expected to be temporary.

13.1.10. Risk from Oxygen Administration

13.1.10.1. There are no 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.

13.1.10.2. 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.

[redacted]

13.1.12. Risk from Loss of Confidentiality

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

13.1.13. Risk from Additional Testing

During the conduct of the study, it is possible, but not likely, that someone could become exposed to the 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), Human immunodeficiency virus (HIV), or Hepatitis C virus (HCV) and additional testing of the sample will be performed.

Within the consent subjects will agree to permit the company to test the blood sample (or samples) by signing the consent. 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.

[redacted]

14. EMERGENCY RESPONSE PLAN FOR MEDICAL EMERGENCIES

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

15. BENEFITS

15.1. There are no other benefits to the subject.

15.2. Other possible benefits would be to society as a whole. Validation of the accuracy of this new device could enable healthcare workers to more appropriately treat potentially life threatening conditions.

16. ALTERNATIVES

16.1. The alternative is to not participate in the study.

17. ADDITIONAL

17.1. Device Accountability

[redacted] Device accountability procedure, consistent with [redacted]

17.2. Bibliography

17.2.1. Masimo Corporation maintains a current list of publications for all of its products and technologies. In order to view the most current clinical information, please visit the Clinical Evidence portion of the Masimo website at http://www.masimo.com/cpub/clinical-evidence.htm

18. PROTOCOL DEVIATION AND PROCEDURE TO AMEND PROTOCOL

18.1. Modifications to the protocol, informed consent materials, recruitment materials, or any other materials provided to subjects must be reviewed and approved by the IRB in accordance with [redacted] prior to implementation.

[redacted]

[redacted]