Official Title: Noninvasive Hemoglobin (SpHb) Clinical Validation of INVSENSOR00026 during Hemodilution

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Protocol/Test Procedure Title	Noninvasive Hemoglobin (SpHb) Clinical Validation of INVSENSOR00026 during Hemodilution
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Expected Start Date	
Expected End Date	
IRB	E&I West Coast Board – IRB00007807
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Protocol Test Abstract:

This study involves evaluating the accuracy of using Masimo's INVSENSOR00026 Pulse CO-Oximeter and Sensor to measure hemoglobin, as compared to hemoglobin measurements obtained from various lab analyzer(s). The performance of the sensors will be calculated using arithmetic root mean square (ARMS) analysis of the SpHb values and the reference blood values. Blood samples will be collected from healthy volunteers who undergo a hemodilution procedure wherein blood is repeatedly sampled as the concentration of hemoglobin is reduced by administering intravenous fluids to the volunteer in a controlled manner.

APPROVALS

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

STATEMENT OF COMPLIANCE

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, federal and local regulatory requirements , 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812, ISO-14155, and International Conference on Harmonisation Good Clinical Practice (ICH GCP).

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. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1. PURPOSE

The primary objective of this clinical investigation is to evaluate the accuracy of using Masimo's INVSENSOR00026 Pulse CO-Oximeter and Sensor to measure hemoglobin, as compared to hemoglobin measurements obtained from various lab analyzer(s). Data using the noninvasive devices will be collected from healthy volunteers undergoing a hemodilution procedure.

This is a nonrandomized single arm study wherein all subjects are enrolled into the experimental arm and receive the INVSENSOR00026 Pulse CO-Oximeter and sensor. Hemodilution will be conducted by delivery of intravenous fluids in a controlled manner to reduce the subject's blood concentration of hemoglobin to obtain noninvasive hemoglobin readings SpHb at various levels. Reference blood samples will be repeatedly collected from the subject and analyzed using a standard laboratory hematology analyzer. The performance of the sensors will be calculated using arithmetic root mean square (ARMS) analysis of the SpHb values and the reference blood values.

Outcome Measure: Performance of INVSENSOR00026 by ARMS calculation

Performance of the Pulse CO-Oximeter and sensors will be determined by comparing the noninvasive hemoglobin measurement (SpHb) of INVSENSOR00026 to the hemoglobin value obtained from a reference blood sample and calculating the ARMS value.

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.

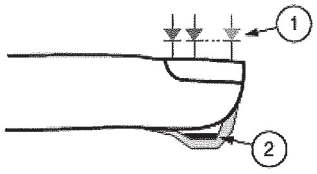
A blood sample gives the best measure of hemoglobin as well as other blood solutes but is difficult to measure continuously and without skin puncture and risk of infection. Masimo SET and Masimo Rainbow technology allows real-time, non-invasive monitoring of hemoglobin (and other blood solutes) in patients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

- Oxyhemoglobin (oxygenated blood) and deoxyhemoglobin (non-oxygenated blood) differ in their absorption of red and infrared light (spectrophotometry).
- The amount of arterial blood in tissue changes with arterial pulses (photoplethysmography). Therefore, the amount of light absorbed by the varying quantities of arterial blood changes as well.

- 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

- Signal data is obtained by passing various [redacted] lights through a capillary bed (for example, a fingertip, a hand, a foot) and measuring changes in light absorption during the blood pulsatile cycle. The detector receives the light, converts it into an electrical signal. Once the oximeter receives the signal from the sensor, it utilizes Masimo Rainbow signal extraction technology for calculation of the patient's hemoglobin level.

2.2. STUDY DEVICES

Investigational sensor: INVSENSOR00026 (Pulse CO-Oximeter and sensor)

The devices used in this study are manufactured per Good Manufacturing Practice (GMP) with traceability of lot or serial numbers and will be labeled as investigational devices, for clinical research only. Final marketed names for the sensor and/or device may change.

The INVSENSOR00026 is a system composed of a handheld Pulse CO-Oximeter and sensor with Rainbow technology similar to already cleared Masimo noninvasive Pulse CO-Oximeters and sensor. The system is intended for spot-check measurements on patients in various care area settings (hospitals, hospital-type facilities, and clinics). The device is a more compact version of already 510(k) cleared Rad-57 and Pronto devices. The Pulse CO-Oximeter device also comes with an upgraded display with touchscreen capabilities. The INVSENSOR00026 Pulse CO-Oximeter and sensor are connected by an accessory patient cable.

The reusable INVSENSOR00026 sensor is intended to measure non-invasive physiological parameters such as SpO2, SpHb, PR, and PI, similar to the existing FDA cleared Masimo rainbow reusable sensors. The sensor has a slimmer and more compact design compared to other Masimo reusable finger sensors. The sensor is intended to be used on patients weighing greater than 3 kg.

3. REFERENCE

[redacted]

[redacted]

4. LOCATION

Masimo Corporation

Clinical Laboratory

52 Discovery

Irvine, CA 92618

[redacted]

5. STUDY POPULATION

5.1. Inclusion Criteria

- Subject is 18 - 50 years of age.
- Subject weighs a minimum of 110 lbs and no more than 250 lbs unless subject is over 6 feet tall.
- Hemoglobin value is greater than or equal to 11 g/dL at time of screening
- Baseline heart rate ≥ 45 bpm and ≤ 85 bpm.
- CO value ≤ 2.0% FCOHb
- Subject has a physical status of ASA I or II (American Society of Anesthesiology Class I; Healthy subjects without any systemic disease at all. American Society of Anesthesiology Class II; subjects with mild systemic disease) as it applies to the systemic disease portion of the classification.
- Systolic Blood Pressure ≤ 140 mmHg and Diastolic Blood Pressure ≤ 90 mmHg.
- Subject is able to read and communicate in English and understands the study and risks involved.

5.2. Exclusion Criteria

- Subject is pregnant
- Subject smokes (including e-cigarette use)
- Subject has a BMI > 35 and has been classified as morbidly obese or at an increased risk for participation by a medical professional.
- Subject has a history of fainting (vasovagal), blacking out or losing consciousness during or after a blood draw.
- Subject has open wounds, inflamed tattoos or piercings, or any visible healing wounds.
- Subject has known drug or alcohol abuse or uses recreational drugs.

- Subject has experienced a head injury with loss of consciousness within the last year.
- Subject has taken anticoagulant medication within the last 30 days.
- Subject has any chronic bleeding disorders (i.e. hemophilia).
- Subject has any history of a stroke, myocardial infarction, heart attack, or seizures.
- Subject has any cancer or history of cancer (not including skin cancer).
- Subject has a chronic neurological disease (i.e. multiple sclerosis, Huntington's disease).
- Subject has any cardiac dysrhythmias (i.e. atrial fibrillation) and has not received clearance from their physician.
- Subject has known neurological and/or psychiatric disorder (i.e. schizophrenia, bipolar disorder) that interferes with the subject's level of consciousness.
- Subject has Wolff-Parkinson-White Syndrome or Stokes-Adams Syndrome
- Subject has any medical condition which in the judgment of the investigator and/or medical staff, renders them ineligible for participation in this study (Discretion of investigator).
- Subject has taken opioid pain medication within 24 hours of start of study.
- Subject has any type of infectious disease (i.e. 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.
- Subject has 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.
- Subject has symptoms of congestion, head colds, flu, or other illnesses
- Subject has donated blood within the last 2 weeks.
- Subject is claustrophobic or has generalized anxiety disorder.
- Subject has been in severe car accident(s) or a similar type of accident(s) requiring hospitalization within the last 12 months.
- Subject has had a concussion within the last 12 months.
- Subject has chronic unresolved asthma, lung disease or respiratory disease.
- Subject is allergic to lidocaine, latex, adhesives, or plastic.
- Subject has heart conditions, 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 last 6 months.
- Subject intends 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 that involves an arterial line.
- Discretion of investigator/study staff

5.3. Withdrawal of subjects

Subjects must be withdrawn under the following circumstances:

5.3.1. The subject withdraws consent.

5.3.2. Discretion of investigator, for example: the investigator feels that the subject is too money motivated, the investigator feels that the subject does not fully comprehend and understand the consent form, the subject is ill-mannered and/or shows aggressive behavior towards study staff,

malfunction of the device for greater than 30 minutes that prevents accurate collection of optical data.

5.4. Replacement of subjects

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

6. 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
- A-line pressure transducer
- Electrocardiogram (ECG)
- Masimo Pulse Oximeters (Radical-7) - for subject safety monitoring
- Pulse oximeter sensors and cables (Masimo SET, Masimo rainbow)
- Masimo Patient Monitoring Platform (Root®)- for subject safety monitoring
- Medical-grade Oxygen tank and mask
- Crash cart

Test Devices

- Masimo INVSENSOR00026 pulse co-oximeter and sensor – Investigational

Research Equipment

- Laboratory co-oximeters/blood analyzers
- Laboratory hematology analyzers

7. PROCEDURE

7.1. SCHEDULE OF ACTIVITIES

Procedures	Phone Pre-Screen	Baseline Visit 1	Procedure Visit 1
Brief Study Procedure Description	X		
Informed consent		X	
Demographics (including skin tone)	X	X	
Medical history (subject-reported)	X	X	
Concomitant medication review	X	X	
Vital Signs (ECG, Blood Pressure Cuff, Pulse Ox)		X	X
Height	X	X	
Weight	X	X	
ASA Status Assessment		X	
Pregnancy test[1]		X	
Allen's Test		X	
Venous sample (via needle stick or IV placement)		X	

Procedures	Phone Pre-Screen	Baseline Visit 1	Procedure Visit 1
Local anesthetics (lidocaine, ethyl chloride spray, or pain ease skin refrigerant) as needed[2]		X	X
Peripheral Venous Line (IV)[2]		X	X
Intra-arterial catheter (A-line)			X
Placement of test and control sensors			X
Noninvasive data collection			X
Removal of Blood (if necessary)			X
IV Fluid Administration			X
Continuous A-line sampling			X
Line Removal			X
Post Care Instructions Given		X	X
Discharge		X	X
Adverse Event Review and Evaluation[3]		X	X

1 hCG (urine) pregnancy test (all female subjects)

2 IV may be placed during screening/baseline to obtain qualifying venous sample at discretion of medical staff. If the IV is placed during screening/baseline, medical staff will offer to use local anesthetics.

3 Adverse events may be reported by the subject after their visit. See section 10 for additional details.

7.2. RECRUITMENT AND PRESCREENING

Subjects will be recruited using IRB-approved advertisements. Subjects may be referred to the study by previous volunteers. Subjects are contacted via phone call to conduct a prescreening interview to determine their initial eligibility for the study. Potential eligible subjects are scheduled for a study visit to the clinical laboratory.

7.3. CONSENTING AND SCREENING

7.3.1. Study staff will discuss the informed consent process and the study with the potential subjects. The subjects will be provided with enough time to read and understand the informed consent document and their questions will be answered by study staff prior to the subject signing the informed consent form. No study related activities will be conducted until consent is signed. If the subject fails to provide proper documentation on their individual consent form for any study, Masimo has the right to re-contact the subject and ask them to return to the clinical lab in order to properly complete the consent form or subject bill of rights.

7.3.2. The subject's weight and height are self-reported, however if the subject appears to be outside the weight range based on the inclusion/exclusion criteria, the subject will be weighed on a scale for verification.

7.3.3. Subjects will be asked to provide a copy of their valid government photo ID and/or Social Security card (SSN) to verify subject identity. The copies of these forms of identification will be stored along with the subject's consent. The confidentiality and retention of these documents will be protected to the extent provided and required by law.

7.3.4. 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.

7.3.5. Subject demographic information including age, sex, skin tone, ethnicity, height and weight will be collected. These may be recorded for data analysis and/or subject safety monitoring purposes.

7.3.6. In addition, a medical history will be recorded after the initial screening questionnaire.

7.3.7. Pre-procedure vital signs will be recorded for subject safety monitoring. Spikes 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. Only the initial recorded blood pressure and/or heart rate determines a subject's qualification for the study.

7.3.8. 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.

7.3.9. A venous sample will be obtained via needle stick or by placement of an IV and analyzed to verify that the subject meets the inclusion criteria for hemoglobin level. The subject will be excluded from the study if the values from the blood draw fall outside the ranges stated in the inclusion criteria.

7.3.10. Subjects may have a blanket placed on them or hot water bottles placed under their hands.

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

7.4. PROCEDURES

7.4.1. Standard hospital-type monitors will be placed on the subject, including ECG and blood pressure, for safety monitoring by medical staff. The procedure will be stopped if there is any evidence of volunteer stress or distress. These signs include but are not limited to a rise or fall in mean arterial blood pressure of more than 30% from baseline, a rise in heart rate to more than 130 BPM, complaints of feeling faint, chest discomfort, GI distress, urinary discomfort or feelings of a bloated bladder, or alternation of mental status. Blood samples are also monitored for hemoglobin and/or blood oxygenation levels for subject safety.

7.4.2. A peripheral venous line will be placed in the volunteer's hand or arm. One or more venous sampling catheters will be used during the study for the removal of blood and administration of fluids.

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

7.4.4. After intravenous access is established, one or more intra-arterial catheter(s) (arterial line or A-line) will be placed in the radial artery of the volunteer's wrist. The A-line is placed to facilitate continuous blood pressure measurement for subject safety monitoring, to enable repeated removal of blood aliquots for reference hemoglobin values, [redacted]

7.4.5. After arterial access is established, optical sensors for the noninvasive measurement(s) will be placed on the subject's fingers.

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

7.4.7. [redacted].

7.4.8. Following removal of blood, the volunteer will rapidly receive intravenous fluid [redacted]

7.4.9. [redacted].

7.4.10. [redacted] blood samples [redacted] will be drawn at selected time intervals throughout the study while intravenous fluid is being administered for laboratory analysis of hemoglobin concentration. [redacted]

7.4.11. The total amount of blood removed from the subject may be up to [redacted]

7.4.12. [redacted].

7.4.13. The hemodilution procedure will continue until the subject's fluid limits have been reached [redacted] or the target hemoglobin value has been reached.

7.4.14. At the conclusion of the procedure, the sensors/devices, IV(s) 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.

7.4.15. At the end of the hemodilution procedure, if the last arterial blood draw hemoglobin value is below 8.0 g/dL, then the subject's hemoglobin level will be monitored using an FDA cleared pulse oximeter. Subjects who have a hemoglobin level below 8.0 g/dL must remain in the study area for observation and meet a minimum rise in hemoglobin of 0.5 g/dL prior to leaving the study area, or until medical staff determines it is safe to do so. If medical staff finds it is not safe to do so, the subject will be referred to an urgent care facility.

7.4.16. 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. Subjects who are employees of Masimo will be advised to take as much time as they need after the study before returning to work.

7.4.17. Volunteers will be given instructions on wound care. All volunteers will be instructed to contact the principal investigator in the event of any potential complication.

7.4.18. The total time for the study procedures will be up to [redacted]. Volunteers will be paid according to the compensation breakdown on the consent form.

7.4.19. 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.

7.4.1 After the study has ended subjects will be offered a snack (eg. Granola bar) and something to drink (eg. 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 line placement. Subjects may also be asked to wait in the clinical lab or lobby waiting area for an additional 30 minutes (estimate) before leaving to allow for their body to continue adjusting after the study has completed.

8. ACCEPTANCE CRITERIA (JUSTIFY IF NOT APPLICABLE)

The pulse co-oximeter and sensors will be determined to have equivalent performance based on the agreement of their ARMS values.

9. SAMPLE SIZE JUSTIFICATION AND DATA ANALYSIS PROCEDURE TO BE USED

9.1. Sample size determination

Sample size for this study has been determined to be [redacted] based on previous experience with similar devices and Masimo internal procedures for sample size calculation and justification ([redacted]).

9.2. Statistical Analysis

Accuracy will be reported as the root mean squared error (ARMS) of the SpHb-tHb parameter. Per ISO 80601 Part 2-61, accuracy of existing pulse oximetry instruments will be reported using ARMS standard calculations which are also applicable to SpHb testing.

$$Bias = \frac{1}{n}\sum_{i=1}^{n}(SpHb - tHb)$$

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

9.3. Measures taken to minimize/avoid bias:

9.3.1. Sensors and devices will be provided to operators in a way that minimizes the operator bias. Sensors and devices will be provided at random when deemed necessary.

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

9.4. Expected drop out rates

Subjects may not complete the study for various reasons, such as screen failure, unable to complete hemodilution criteria, unable to have intravenous or arterial line placed. [redacted]

10. ADVERSE EVENTS

Definitions:

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.

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 will be reported and documented as described below.

10.1. Adverse Events

All adverse events that occur during the study shall be recorded on the Case Report Form even if the investigator assesses the adverse event as unlikely to be causally related to the test device or study procedures. The investigator will inform the sponsor and IRB as required by IRB reporting guidelines.

10.2. Serious Adverse Events

10.2.1 The investigator/study staff shall promptly report both serious adverse events (e.g., subject death, subject hospitalization for several days) 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.

10.2.2 At the time of discharge from the study, any unresolved serious adverse event(s) will be followed up by the investigator until the event(s) are resolved, stabilized or the patient is lost to follow-up or the adverse event is otherwise explained. The investigator 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.

10.3. Unanticipated Problems

Any unanticipated problem involving subjects or others will be reported to the IRB, such as protocol violations or deviations as required by the IRB reporting procedures.

11. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

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

11.1.1. 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.

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

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

11.1.2.2.Only their corresponding identification number will identify subjects.

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

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

11.2. Vulnerable Populations

11.2.1. Employees are considered to be a vulnerable population.

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.

11.2.2. Economically disadvantaged or unemployed and educationally disadvantaged

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.

11.3 Documents and Database

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

Documents and information stored electronically will be protected using a multi-faceted procedure including, but not limited to the following steps:

- Two layers of endpoint security and one layer of DLP (Data loss prevention) running on all company machines.
- Premier firewalls/Network monitoring appliances and log collection systems (SIEM) protecting the network.
- 4 layers of email security systems for protecting against phishing attacks.
- Security policies to limit access to specific folders.

12. DEVICE ACCOUNTABILITY

12.1. Receipt of Study Device

Upon receipt 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.

12.2. Use of Study Device

Use of devices and sensors will be documented on case report forms for each subject.

12.3. Return or Destruction of Study Device

At the completion of the study, there will be a final reconciliation of study devices and sensors shipped, devices/sensors used, and devices/sensors 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.

13. RISKS AND BENEFITS

13.1. Benefits: There would be no other benefit to the subject. Other possible benefits would be to society as a whole. Evaluation of the accuracy of this new device could enable healthcare workers to more appropriately treat potentially life threatening conditions.

13.2. 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 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).

13.3. Venous Cannulation Risks: bleeding, swelling, infection, infiltration of fluids/ blood into area surrounding IV, bruising, hematoma, damage to the blood vessel and surrounding nerves or tissue.

13.4. Arterial Cannulation risks: 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.

13.5. Risks Associated with Removal of Blood: Removal of blood is generally considered to be safe in most patients and exceptionally safe in healthy volunteers (i.e. blood donation). The risk of removing blood includes the risks obtaining venous access. Additionally, there is the risk of hypotension, tachycardia, anemia, dizziness and loss of consciousness. All subjects will be maintained in a reclined position throughout the study and a physician will be available to continually monitor the vital signs.

13.6. Blood Draw risks: discomfort is generally associated with needle puncture. The most common complications associated with blood draws and capillary sticks are hematomas or bruising. All blood draws will be performed by qualified personnel. An ACLS certified physician will be in attendance throughout the entire procedure, and the study will be completed under their general supervision. Other anticipated adverse events that may occur, include but are not limited to: Vaso vagal (passing out), infiltrated IV, 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 sweating, and mouth dryness. These anticipated adverse events are expected to be temporary.

13.7. Risk From Hemodilution: Hemodilution has been used successfully as a technique to reduce perioperative blood loss during surgery. Hemodilution is generally considered to be safe in most patients and exceptionally safe in healthy volunteers. In surgery, the chief benefit of hemodilution is the reduction of blood losses when whole blood is shed perioperatively at lower hematocrit levels after hemodilution is completed. In our controlled clinical lab, withdrawal and blood loss will be limited to samples required for laboratory analysis; hemodilution will be used principally to lower the subject's hematocrit and hemoglobin. The risks of hemodilution include heart failure, respiratory failure, hypertension, edema, infection and electrolyte abnormalities. Isotonic fluids will

be administered. A physician will be immediately available thorough out the procedure and vital signs will be continually monitored.

13.8. Risk from Inflicted Knowledge: The risk of inflicted medical knowledge to volunteers is negligible since we deidentify 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. Subjects are informed that these are not diagnostic tools, if observations are made using FDA cleared devices we will refer them to their primary care physician.

13.9. 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.

13.10. 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.

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.

13.11. Lidocaine (injection) Risks: Insertion 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. These adverse events are expected to be temporary.

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

13.13. Ethyl Chloride (Lidocaine Spray): Ethyl Chloride is a topical anesthetic which is 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 (i.e. Flushing or redness of the skin), delayed wound healing, rash, itching and swelling. These adverse events are expected to be temporary.

14. 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 volunteer with the ACLS approved protocol for intervention. A crash cart is on site and full emergency services are within 3 miles.

15. MONITORING PLAN

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

16. PROTOCOL DEVIATIONS AND AMENDMENTS

Deviations to the protocol will be documented on the Case Report Form or a separate document. Protocol deviations will be reported to the sponsor and IRB per IRB reporting guidelines.

Modifications to the protocol, informed consent materials, recruitment materials, or any other materials provided to subjects must be reviewed and approved by the IRB.