Official Title: Desaturation Validation of INVSENSOR00009

Date of Protocol: November 21, 2017

NCT Number: NCT03396835

MASIMO

PROTOCOL/TEST PROCEDURE

[redacted]

Desaturation Validation of INVSENSOR00009

Protocol/Test Procedure Title	Desaturation Validation of INVSENSOR00009
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Expected Start Date	
Expected End Date	
IRB	E&I West Coast Board – IRB00007807
Protocol Version Date	TBD

Protocol Test Abstract:

This study is designed to measure the trending accuracy of a noninvasive measurement of cerebral oxygen saturation. One Large sensor (adult sensor) and one INVSENSOR00009 will be placed on the subject's forehead. The values obtained by the INVSENSOR00009 will be compared to the values collected with the adult sensor. Data will be collected from healthy adult subjects while undergoing a desaturation procedure wherein the concentration of oxygen inhaled is slowly reduced [redacted]. The subject will then be returned to inhaling room air.

APPROVALS

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

[redacted]

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, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812, ISO-14155, and International Conference on Harmonisation E6 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.

1. PURPOSE

This study is designed to measure the trending accuracy of a noninvasive measurement of cerebral oxygen saturation. One adult sensor[1] and one INVSENSOR00009 will be placed on the subject's forehead. The adult sensor has been tested for accuracy with respect to invasive blood gases and is approved for clinical use in the US and EU.

[redacted] The INVSENSOR00009 is not approved for clinical use and is considered an investigational device. The values obtained by the INVSENSOR00009 will be compared to the values collected with the adult sensor.

This is a nonrandomized single arm study wherein all subjects are enrolled into the experimental arm and have the INVSENSOR00009 sensor and adult sensor placed on the forehead. Data using the noninvasive devices will be collected from healthy volunteers undergoing a desaturation procedure. Desaturation will be conducted by reducing the concentration of oxygen the study subject breathes in a controlled manner to obtain noninvasive oxygen saturation readings, rSO_2, at various levels. [redacted] The adult sensor is considered the Control sensor in this study.

Outcome Measure:

This study will evaluate the Trending accuracy of the INVSENSOR00009 relative to the adult sensor.

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.

2.1. Technology Background

Regional oximetry is a noninvasive technology for measuring the level of oxygenation in deep tissue (rSO2). To arrive at their measurements, regional oximeters use Near Infrared Spectroscopy (NIRS), which is based on the Beer Lambert Law.

[1] Masimo O3 Large Sensor [redacted]

For cerebral oximetry, multiple detectors and emitters are utilized to provide multiple pathways for the light to travel through the tissue. Software algorithms then process the received light signals to provide an oxygenation measurement.

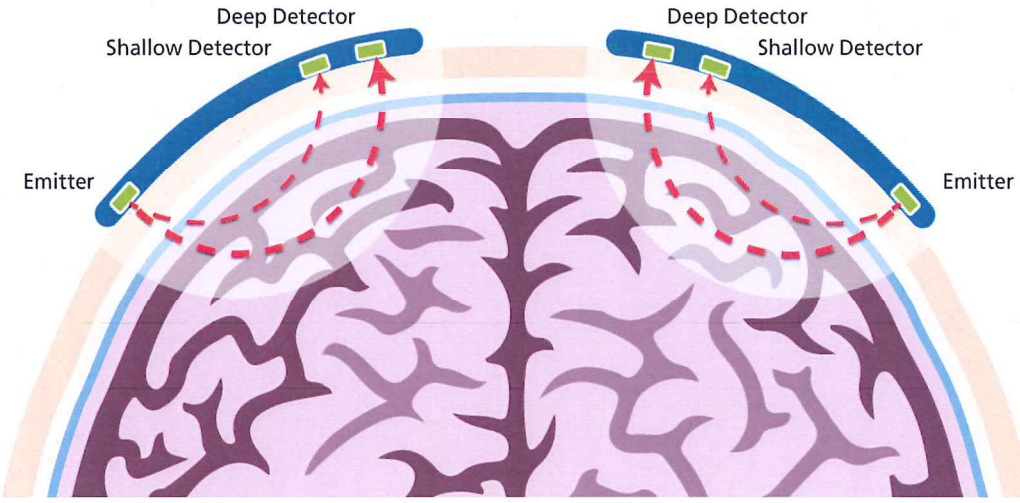


Figure 1: Schematic of two regional oximeter sensors measuring deep tissue oxygenation.

2.2. Study Devices

Investigational sensor: INVSENSOR00009

The INVSENSOR000009 sensor is a modification to Masimo's O3 adult line of sensors. [redacted]

FDA Cleared Sensors and Devices:

Masimo Root Patient Monitoring Platform: Root is a patient monitoring and connectivity platform that offers rainbow® and Masimo SET® measurements with other parameters in an integrated platform. With docking capabilities for the Radical-7® handheld monitor and multiple networking/connectivity options, Root integrates multiple streams of data into one display monitor.

The Masimo O3 module and adult Sensor are cleared for clinical use on adults in US and EU countries. The approved O3 module will be installed in the Root monitor and used to collect data from both the adult and INVSENSOR00009 sensors during this study.

3. REFERENCE

[redacted]

4. LOCATION

Masimo Corporation

Clinical Laboratory

52 Discovery

Irvine, CA 92618

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 routine required 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.

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.
- 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 (smoking includes 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 open wounds, inflamed tattoos or piercings, visible healing wounds.
- Subject experiences frequent or severe headaches and/or migraine headaches.
- Subject has known drug or alcohol abuse and/or use of recreational drugs.
- Subject has experienced a concussion or head injury with loss of consciousness within the last year.
- Subject has any chronic bleeding disorders (i.e. hemophilia).
- Subject has any history of a stroke, myocardial infarction, seizures or heart attack.
- 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 dysrhythmia(s) (i.e. atrial fibrillation) and has not received clearance by their physician to participate.
- Subject has a known neurological and/or psychiatric disorder (i.e. schizophrenia, bipolar disorder) that interferes with the subject's level of consciousness.
- 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 Wolff-Parkinson-White Syndrome or Stokes-Adams Syndrome.
- Subject who has taken anticoagulant medication within the last 30 days.
- Subject has taken opioid pain medication within 24 hours of start of study.
- Subject has either signs or history of peripheral ischemia.
- 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 donated blood within the past 30 days.
- Subject has symptoms of congestion, head colds, flu or other illnesses.
- Subject experiences claustrophobia 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 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 given vaginal delivery, had a pregnancy terminated, a miscarriage with hospitalization, or had a C-section within the last 6 months.
- 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.
- Subject displays or communicates signs of discomfort or distress so that the study may not be continued.

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
- Electrocardiogram (ECG)
- Masimo Pulse Oximeters (Radical-7)
- Masimo Patient Monitoring Platform (Root®)
- Pulse oximeter sensors and cables (Masimo SET, Masimo rainbow, or comparable)
- Medical-grade oxygen tank and mask
- Crash cart

Test Devices

- Masimo INVSENSOR00009

Control Devices

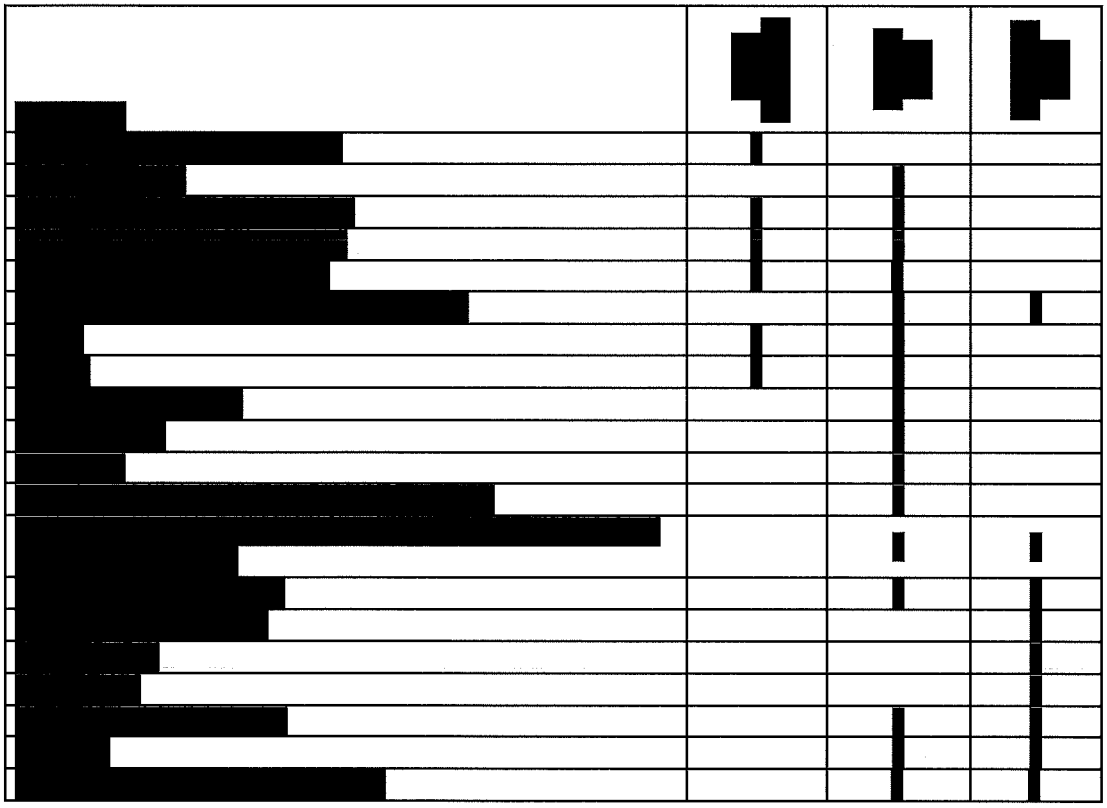
- Masimo O3 Large Sensor [redacted] ("adult sensor")

Research Equipment

- Masimo Patient Monitoring Platform (Root®)
- O3 Regional Oximeter Module [redacted]
- Passive Data Collection Research Equipment [redacted]

7. PROCEDURE

7.1 SCHEDULE OF ACTIVITIES



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 subjects. 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.

7.3.2. The subject's weight and height are self-reported, however the subject may 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 Number (SSN) card 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 must meet all the inclusion criteria and none of the exclusion criteria in order 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 and HbCO. 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 for their comfort.

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, blood pressure, and a reference pulse oximeter for safety monitoring by medical staff.

7.4.2 Proprietary Masimo data collection software will be used to verify all oximeters are reading. If not, proper sensor positioning will be checked and sensors may be repositioned, as needed.

[redacted]

7.4.3 A peripheral venous line will be placed in the subject's hand or arm. This line may be used for the qualifying venous blood draw and for safety or clinical intervention required during the study.

7.4.4 [redacted] 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.

7.4.5 This study does not require arterial blood samples.

7.4.6 The control and INVSENSOR00009 will be placed on the subject's forehead.

[redacted]

7.4.8 [redacted] Upon indication the subject is comfortable, a gas mixture will be administered [redacted] 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 as measured by [redacted] Note: At any point in the study, if the subject feels uncomfortable, the subject will be given 100% oxygen [redacted] mouthpiece or a supplemental mask.

[redacted]

7.4.14 The study will end with several minutes at a FiO_2 greater than room air (>21%) to help the subject re-saturate after the procedures.

7.4.16 At the conclusion of the procedure, the sensors/devices, and IV(s) will be removed and the subject will be allowed to leave after medical personnel determine it is safe to do so.

7.4.17 The total procedure time will be approximately [redacted]

7.4.18 All subjects will be encouraged to remain in the study area until they feel fit to leave.

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

7.4.20 Subjects will be paid for their time.

7.4.21 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.

8. ACCEPTANCE CRITERIA

[redacted]

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

[redacted]

9.2. Statistical Analysis

Sensors are applied to both sides of the forehead, one side with adult sensor, the other side with INVSENSOR00009 sensor. The adult sensor is the Control.

Relative rSO2 is computed on a sensor by sensor basis by subtracting each sensor's mean rSO2 from its rSO2 vector. Relative error is defined to be the relative rSO2 difference of the test sensor and adult sensor. [redacted]

[redacted]

9.3. Measures taken to minimize/avoid bias:

The adult and INVSENSOR00009 sensor will alternate forehead sides (Left or Right) for each subject. For example, Subject 01 will have the adult sensor on the left side. Subject 02 will have the adult sensor on the right side.

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.

9.4. Expected drop out rates

Subjects may not complete the study for various reasons, such as a clinical screening test failure, unable to complete desaturation [redacted], unable to have intravenous 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.

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.

10.1. Adverse Events

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

10.2. Serious Adverse Events

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.

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 and/or 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.

10.3. **Unanticipated Problems**

Any unanticipated problem involving subjects 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

11.3.1 Documents will be kept [redacted] If destroyed, these documents will be shredded and done by a certified company used for destroying medical and clinical data.

[redacted] Documents and information stored electronically will be protected using a multi-faceted procedure including, [redacted]

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 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 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 forehead 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: swelling, infection, infiltration of fluids/ blood into area surrounding IV, bruising, hematoma, lightheadedness, fainting, feeling flush/warm, feeling nauseated, throwing up, 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, damage to the blood vessel and surrounding nerves or tissue.

13.4. Other anticipated adverse events that may occur, include but are not limited to: vasovagal (passing out/fainting), infection to the skin or area right below the skin, 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.

13.5. Risk From Oxygen Administration: 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. Subject's 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.

13.6. Low Oxygen Concentration Risks: Risks associated with hypoxia include dizziness, shortness of breath, drowsiness, or headache. If or when this occurs, the study can be stopped. There is an extremely small risk of loss of consciousness, damage to vital organs, or death from lack of oxygen. The study shall be stopped by the subject or clinical staff long before this could occur. Other anticipated adverse events that may occur, include but are not limited to: vasovagal (passing out/fainting), 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. These anticipated adverse events are expected to be temporary.

13.7. Nose Clip Risks: It is expected that some people will have discomfort/ pinching/ scratches from wearing a nose clip. If this occurs, adjustments can be made and/or the study can be stopped.

13.8. 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 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:

13.11.1. 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.

13.11.2. 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.

13.11.3. 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.

13.11.4. 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. 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.

13.12. 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 subject 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.