Official Title: INVSENSOR00032 and INVSENSOR00033 Respiration Rate Clinical Performance Study

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Protocol/Test Procedure Title	INVSENSOR00032 and INVSENSOR00033 Respiration Rate Clinical Performance Study
Lead Investigator	[redacted] Masimo Corporation 52 Discovery, Irvine, CA 92618
Other Investigators	N/A
Expected Start Date	N/A
Expected End Date	N/A
IRB	E&I West Coast Board – IRB00007807

Protocol Test Abstract:

This study compares the performance of respiration rate from pleth (RRp) measured prospectively with either INVSENSOR00032 and/or INVSENSOR00033 devices against the respiration rate derived from the manual scoring of the capnography waveform (RR_{ref_c}) in healthy adult subjects.

APPROVALS

Author	Date	Engineering	Date
[redacted]	[redacted]	[redacted]	[redacted]
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 Harmonization 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

The objective of this prospective study is to compare the noninvasive respiration rate from pleth (RRp) performance of the INVSENSOR00032 and/or INVSENSOR00033 devices against the manual scoring of the capnography waveform (RR_{ref_c}). All of the devices are noninvasive and the data will be collected from healthy adult subjects.

This is a nonrandomized single arm study wherein all subjects are enrolled into the experimental arm. The subjects will have one or both of the test devices (INVSENSOR00032 and INVSENSOR00033) placed on their fingers along with a nasal cannula attached to a capnography device.

Outcome Measure: Comparison by arithmetic root mean square (A_{RMS}) calculation of respiration rate from pleth (RRp) measured by either one or both of the test devices and respiration rate obtained by manual scoring of the capnography waveform (RR_{ref_c}).

2. BACKGROUND

Masimo Corporation develops noninvasive 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. Background and Rationale

Recording respiratory rate is considered standard for monitoring patients. However, measurement frequency and documentation of respiratory rate is often poor and inaccurate. Respiratory rate is difficult to assess and often is not even recorded in the patient record. This is in spite of the fact that elevated respiratory rate is one of the best predictors of respiratory deterioration, cardiac arrest, and admission to the intensive care unit (ICU). The test devices allow for real-time, non-invasive monitoring of respiration rate in patients and have the potential to improve clinical outcomes while reducing the cost of care and risks to patients.

Respiration rate can be determined by the plethysmographic waveform. This method measures respiration per minute (rpm) based on plethysmographic amplitude and phase changes that correspond to the respiratory cycle.

Literature Review:

1. "Target Heart Rate and Estimated Maximum Heart Rate." Centers for Disease Control and Prevention, CDC, 10 Aug. 2015, www.cdc.gov/physicalactivity/basics/measuring/heartrate.htm.

2. "ASA Physical Status Classification System - American Society of Anesthesiologists (ASA)."American Society of Anesthesiologists, 15 Oct. 2014, www.asahq.org/resources/clinical-information/asa-physical-status-classification-system.

[redacted]

2.2. Study Devices

2.2.1. INVSENSOR00032: The investigational Masimo INVSENSOR00032 is a wearable sensor intended to provide respiration rate values [redacted]

2.2.2. INVSENSOR00033: The investigational Masimo INVSENSOR00033 is a modification of a Masimo FDA-cleared Pulse CO-Oximeter that has been modified to enable measurements of noninvasive respiration rate from pleth (RRp). The INVSENSOR00033 Pulse CO-Oximeter will be connected to the patient using FDA-cleared sensors and cables

2.2.3. FDA cleared Sensors and Devices:

- Masimo FDA-cleared pulse oximeter sensor
- Masimo FDA-cleared Patient Cable

[redacted]

3. REFERENCE

3.1.	[redacted]	Consent to be a Research Subject
3.2.	[redacted]	Recruitment Script
3.3.	[redacted]	Web Ad
3.4.	[redacted]	Health Assessment Questionnaire
3.5.	[redacted]	Case Report Form
3.6.	[redacted]	Confidentiality Agreement
3.7.	[redacted]	Clinical Study Request Form
3.8.	[redacted]	Protocol Deviation Report
3.9.	[redacted]	Adverse Event Report Form
3.10.	[redacted]	Device Accountability Log

[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. All personnel undergo routine required training on GCP and human subject research protections. The laboratory is equipped with standard FDA-approved medical monitoring equipment. Hospitals and urgent care facilities are within three miles of Masimo Clinical Laboratory.

5. EQUIPMENT, AND MATERIALS AND SAMPLE SIZE JUSTIFICATION

5.1. Equipment and Materials

All lab equipment will be maintained per manufacturer specifications and all study personnel will be trained on the use of relevant equipment.

Test Devices:
INVSENSOR00032
INVSENSOR00033

(Reference) Control Devices:
[redacted]

Research Equipment:
Data Collection Laptop, software and other equipment as necessary to record the data
[redacted]

5.2. Sample Size Justification

[redacted]

6. PROCEDURE

6.1. STUDY POPULATION

6.1.1 Inclusion Criteria

- 18 to 70 years old
- Physical status of ASA I or II, refer to [2] in Literature Review
- Must be able to read and communicate in English
- Has signed all necessary related documents, e.g. written informed consent, confidentiality agreement.
- Passed health assessment screening
- Negative pregnancy test for female subjects of child bearing potential.

6.1.2. Exclusion Criteria

- Physical status of ASA III, IV, or V, refer to [2] in Literature Review
- Subject has any medical condition which in the judgment of the investigator, renders them inappropriate for participation in this study
- Inability to tolerate sitting still or minimal movement for at least 30 minutes
- Positive pregnancy test for female subjects
- Refusal to take pregnancy test for women of child bearing potential
- Nursing female subjects
- Subjects wearing acrylic nails or subjects refusing to remove nail polish
- Subjects who have a nail deformity on the measurement finger
- Subjects who do not have adequate skin integrity on the measurement finger
- Excluded at the Principal Investigator's discretion

6.1.3. Withdrawal and Replacement of Subjects

Subjects must be withdrawn under the following circumstances:

- The subject withdraws consent or assent
- Serious adverse event
- Discretion of investigator, for example:
  - The subject is ill-mannered and/or shows aggressive behavior towards the study staff.
  - Subject displays or communicates signs of discomfort or distress so that the study may not be continued
- Malfunction of the device for greater than 10 minutes

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

6.2. Advertisement and Recruitment

6.2.1. Our Web Ad ([redacted]) will be posted publically on craigslist or similar websites.

6.3. Phone Screening

6.3.1. Once the potential subject sees the recruitment material, they contact our clinical schedulers to elicit more details about the screening. The phone screening is handled by designated clinical staff that is trained for screening/scheduling.

6.3.2. Appointments are made once the phone screening process is completed and the person screening the subjects determines they qualify for screening based on the Recruitment Script ([redacted]).

6.3.3. If the person does not qualify at this time the information will not be retained.

6.4. Consent Process.

6.4.1. Have each volunteer read and sign the correct forms which include the consent form ([redacted]) and the Confidentiality Agreement ([redacted]). The consent form must be stamped with current IRB approval. No study related activities will be conducted until consent is signed.

6.4.2. Subject demographic information including age, gender, height, weight, and ethnicity may be collected. In addition, a brief medical history, Massey scale assessment, and vital signs may be recorded.

6.5. Screening:

6.5.1. Have each subject complete [redacted] – Health Assessment Questionnaire.

6.5.2. Female volunteers of child bearing potential will be required to take a pregnancy test as part of screening. A positive pregnancy test will disqualify them from the study.

6.5.3. If the subject does not pass screening, he/she will be not be compensated for travel.

6.6. Study Procedure

6.6.1. Apply the INVSENSOR00032 device on the subject's index, middle or ring finger and [redacted]. Follow the instructions to pair INVSENSOR00032 with a host device.

6.6.2. Apply a pulse oximeter sensor on the subject's other hand's index, middle or ring finger and [redacted] Attach the sensor to the INVSENSOR00033 device.

6.6.3. Put in a flexible tube called a nasal cannula in the subject's nose. The study starts once the first sensor is placed.

[redacted]

[redacted]

6.6.6. Photos may be taken of sensor placement. Photos may only be taken with the subject's consent. All photos will be de-identified and will not show the subject's face or any other identifying features.

6.6.7. Data may be collected while the subject is sitting in a chair or standing still.

[redacted]

6.6.9. Subjects may stop the study at any time.

6.6.10. Subjects will be compensated for their time and discomfort involved in study participation. The study is expected to last less than an hour and they will be compensated [redacted] after completing the study.

6.6.11. Non-disposable devices will be sanitized after each subject completes the study.

6.7. Discontinuation

In the event that a study is discontinued prior to completion, whether it is due to the investigator's discretion or the subject's request, the subject will be paid [redacted]

6.8. Protocol Deviation

If there is a protocol deviation it shall be recorded on the Case Report Form. The Protocol Deviation Report ([redacted]) shall also be completed.

7. ACCEPTANCE CRITERIA

[redacted]

8. DATA ANALYSIS PROCEDURE TO BE USED

8.1. Statistical Analysis

[redacted]

8.1.2. Reference Respiration Rate (RR_{ref_c})

The [redacted] files are used by a [redacted] to establish a reference respiration rate (RR_{ref_c}).

8.1.3. RRp Measurement Values

[redacted]

8.1.4. Analyzing Clinical Performance

Use the paired RRp measurement and RR_{ref_c} reference values to calculate the A_{RMS} based upon the following equations:

Bias	Precision	Arms

$\frac{1}{n}\sum_{1}^{n}(RRp - RR_{ref\_c})$	$\sqrt{\frac{\sum_{1}^{n}((RRp - RR_{ref\_c}) - Bias)^2}{n}}$	$\sqrt{\frac{\sum_{1}^{n}(RRp - RR_{ref\_c})^2}{n}}$

8.2. Expected Dropout Rates

Subjects may not complete the study for various reasons, such as a clinical screening test failure, at the Principal Investigator's discretion, or because the subject does not want to continue the study. Due to the short duration and simple, noninvasive procedures of this study, there are no expected dropouts.

9. 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.

If there is a device deficiency during the study, it will be documented on the Case Report Form, [redacted] and it 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.

10.1 Adverse Events

All devices used in the study are non-significant risk devices. All study procedures are noninvasive. In the unlikely event that an adverse event should occur, it will be reported and documented as described below.

All adverse events that occur during the study shall be recorded on the Case Report Form. The Adverse Event Report Form ([redacted]) shall also be completed.

Skin irritation or redness from the adhesive are anticipated adverse events.

10.2 Serious and Unanticipated Adverse Events

The investigator shall promptly report to the IRB within 24 hours any serious and unanticipated adverse event involving subjects.

At the time of discharge from the study, an unresolved serious and unanticipated adverse event(s) will be followed up by the investigator until the event(s) are resolved, stabilized, or the patient is unable 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 problems involving subjects will be reported to the IRB, such as protocol violations or deviations as required by the IRB reporting procedures.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

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

11.1.1 All subjects will be monitored closely throughout the study.

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

11.1.2.1 Information about the patients will be kept confidential.

11.1.2.2 An identification number (code) for each subject will be kept on file.

11.1.2.3 The study documents will only contain the subject's corresponding identification number except in the Informed Consent Document.

11.1.2.4 Access to identifying documents and data will only be granted to the investigators in the study.

11.1.2.5 Study data that will be released to Masimo and other regulatory authorities will be de-identified and will only pertain to study data collection, demographics, sensor placement locations and recordings from devices.

11.1.2.6 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.

11.2.1.1 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.

11.2.1.2 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.

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

11.2.2.2 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 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.

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

11.3.2.1 Endpoint: 2 layers of endpoint security and one layer of DLP (Data loss prevention) running on all company machines.

11.3.2.2 Premier firewalls/Network monitoring appliances and log collection systems (SIEM) protecting the network

11.3.2.3 4 layers of email security systems for protecting against phishing attacks

11.3.2.4 Security policies to limit access to specific folders

11. DEVICE ACCOUNTABILITY

11.1. Receipt of Study Device

Upon receipt of the study device supplies, an inventory must be performed and the Device Accountability Log [redacted] 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.

11.2. Use of Study Device

Use of devices and sensors will be documented on Case Report Forms for each subject.

12. RISKS AND BENEFITS

12.1. Benefits

There would be no other benefit to the subject. Other possible benefits would be to society as a whole.

12.2. Device Risks

Risks of skin irritation or redness to adhesives. Additionally any adhesive may leave a temporary mark on the subject's skin.

12.3. Risks associated with disclosure of confidential information

There is minimal risk to the privacy of the subject because access to study data will be kept in a secure location and limited to study personnel and to others legally authorized to view it.

12.4. Risks associated with study procedures

There is minimal risk. The study procedures involve the subject changing their respiratory rate and doing moderate exercise.

13. EMERGENCY RESPONSE PLAN FOR MEDICAL EMERGENCIES

A crash cart is on site and emergency services are available within a 3 mile radius of the facility.

14. MONITORING PLAN

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

15. PROTOCOL DEVIATIONS AND AMENDMENTS

Deviations from 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.