NCT06149416

Post-launch Hypoxia Clinical Study Protocol for Reprocessed Masimo RD SET Pulse Oximeters with Motion

May 25, 2023

General Information

1.0 Purpose

1.1 The purpose of this clinical study is to validate the SpO2 accuracy of the Stryker Sustainability Solutions pulse oximetry sensors during motion conditions over the range of 70-100% SaO2 as compared to arterial blood samples assessed by CO-Oximetry during conditions in which the subject is moving. The end goal is to provide supporting documentation for the SpO2 accuracy validation of the reprocessed sensors with motion indications.

In this study, the level of oxygen within the blood will be reduced in a controlled manner by reducing the concentration of oxygen the study volunteer breathes. The accuracy of a noninvasive pulse oximeter sensor will be assessed by comparison to the oxygen saturation measurements from a laboratory blood gas analyzer.

A machine will be used to induce motions of 20 mm during testing at a sine rate of 2Hz, 3Hz, and 4Hz. A third motion moves the arm a random distance of 0 to 30mm at a random speed up to 5Hz.

It is required that the Accuracy Root Mean Square (ARMS) performance of the Stryker pulse oximetry sensors will meet a specification of +/-3% with a target of +/-3% or better in motion conditions for the range of 70 - 100% SaO2 (typically, saturation is determined once with air breathing and then at three or six levels, e.g. 94%, 90%, 85%, 80%, 75% and 70% or 95%, 85% and 75% saturation for about 30-60 seconds or 60-90 seconds at each level), thereby demonstrating an acceptable SpO2 accuracy performance specification. This study should utilize a three level structure (95%, 85% and 75%).

1.2 This study is being conducted to support a modification to the regulatory body approval of pulse oximeter probes reprocessed by Stryker Sustainability Solutions.

2.0 Scope

2.1 This procedure applies to the following Stryker Sustainability Solutions location(s):

☒ Tempe ☐ Phoenix ☐ Lakeland ☒ Tijuana ☐ Chandler

2.2 This study has been designed to include the subject devices listed in Table 1.

Study Device:			
OM	SKU	Minimum Quantity	Cycle Count
Masimo	4000 Adt (Adult)	10	4x
Masimo	4003 Neo (Adult & Neonate)	10	4x

Table 1: Subject devices

3.0 Associated References

3.1 Pulse Oximeters – Premarket Notification Submissions [510(k)s] Guidance for Industry and Food and Drug Administration Staff Document issued on: March 4, 2013

3.2 ISO 80601-2-61:2019 Medical Electrical Equipment — Part 2-61: Particular requirements for basic safety and essential performance of pulse oximeter equipment

4.0 Related Documents

4.1 DWI-CDS-109, Division Engineering Study Templates

4.2 DWI-CDS-112, Division Engineering Study Exceptions
4.3 DWI109.650, New Product Development Training Form
4.4 CRD10352, Post Launch Hypoxia Clinical Study Report for Reprocessed Masimo RD SET Pulse Oximeters with Motion
4.5 TR22597, Post Launch Sample Preparation Report for Reprocessed Masimo RD SET Pulse Oximeters
4.6 CQD-CCA-001 Conducting Clinical Research
4.7 CQP-CCA-002 Approval of Clinical Research Proposals, Protocols, Study Design Documents and Publications
4.8 DSOP587 Division Conducting Clinical Research
4.9 D0000065949 Investigator Initiated Studies
4.10 DP-MCF-001, Division Complaint Handling Process
4.11 DP-CDS-013, Risk Management

5.0 Key Terms

Refer to CQM-02, Stryker Corporation Quality and Regulatory Master Glossary, for definitions to the Key Terms used within this document.

5.1 Allocation: A method used to assign participants to an arm of a clinical study. The types of allocation are randomized allocation and nonrandomized.
5.2 Arm: A group or subgroup of participants in a clinical trial that receives a specific intervention/treatment, or no intervention, according to the trial's protocol.
5.3 Eligibility criteria: The factors that allow someone to participate in a clinical study are called inclusion criteria, and the factors that disqualify someone from participating are called exclusion criteria. They are based on characteristics such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions.
5.4 Intervention/treatment: A process or action that is the focus of a clinical study. Interventions include drugs, medical devices, procedures, vaccines, and other products that are either investigational or already available. Interventions can also include noninvasive approaches, such as education or modifying diet and exercise.
5.5 Masking: A clinical trial design strategy in which one or more parties involved in the trial, such as the investigator or participants, do not know which participants have been assigned which interventions. Types of masking include: open label, single blind masking, and double-blind masking.
5.6 Primary outcome measure: In a clinical study's protocol, the planned outcome measure that is the most important for evaluating the effect of an intervention/treatment. Most clinical studies have one primary outcome measure, but some have more than one.
5.7 Study type: Describes the nature of a clinical study. Study types include interventional studies (also called clinical trials), observational studies (including patient registries), and expanded access.

6.0 Roles and Responsibilities

6.1 Divisional

6.1.1 R&D Engineering in collaboration with Advanced Quality Engineering and Regulatory Affairs is responsible for the preparation and execution of this protocol, analysis of the test results, and the preparation of the summary report.

6.1.2 R&D Engineering, Advanced Quality Engineering, and Principal Investigators are responsible for ensuring adherence to the Clinical Trial Agreement associated with the study outlined in the protocol.

6.1.3 The external facilities that may be used in the execution of this protocol are listed in Table 2.

Service	Name and Location
Clinical Study	UCSF (University of California San Francisco) 490 Illinois Street, 5th Floor San Francisco, CA 94143-1209

Table 2: Test laboratory name and address

Procedure

7.0 Summary

Study Design:	
Study Type:	Interventional Non-significant Risk Lab Test
Enrollment:	A typical study will include at least 10 subjects (up to 24 if needed to reach the 200 necessary data points to meet the ISO 80601-2-61:2019).
Allocation:	Non-randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	Subjects will recline for the study. Reference sensors will be placed on each subject to evaluate the SpO_2 accuracy and performance. Shield material may be used between any adjacent finger sensors to prevent optical crosstalk. A machine will be used to induce motions of up to 20 mm during testing at a sine rate of 2Hz, 3Hz, and 4Hz. A third motion moves the arm a random distance of up to 30mm at a random speed up to 5Hz. Simultaneous data collection will be set up for devices under test. The data from the test devices will be collected by the sponsor or trained UCSF staff. Data will be collected for 1 second intervals data analysis. The SpO_2 accuracy of the test devices will be evaluated over the oxygen saturation range between 70-100%.
Masking:	None (Open Label)
Primary Purpose:	Device Validation
Study Start Date:	May 27-28, 2023

Arms and Interventions:	
Experimental: Masimo RD SET SpO2 Adhesive Sensors, Adult (4000 Adt), Adult & Neonate (4003 Neo) Reference sensors from the reprocessed oximeter device will be placed on each subject to evaluate the SpO2 accuracy and performance.	Device: Stryker Sustainability Solutions Reprocessed Masimo RD SET Pulse Oximetry Sensors An oximeter is a device used to transmit radiation at a known wavelength(s) through blood and to measure the blood oxygen saturation based on the amount of reflected or scattered radiation. Pulse oximetry monitoring is considered a standard physiological measurement and is used by clinicians in everyday situations to estimate arterial oxygen saturation. Because an arterial sample of blood is not required to make the measurement, the pulse oximeter can provide non-invasive real time information.

Sham Comparator: Radiometer ABL-90 multi-wavelength oximeter A whole blood analyzer (CO-Oximeter) is used as the reference standard device for obtaining the functional SaO2 value from arterial blood samples obtained during the study.	Device: CO-OXIMETRY SENSORS A whole blood analyzer (CO-Oximeter) is used as the reference standard device for obtaining the functional SaO2 value from arterial blood samples obtained during the study.
Primary Outcome Measures:	
1. Accuracy of Sensor by Arms Calculation [Time Frame: 1-5 hours]	Percentage of SpO2 (oxygen saturation by pulse oximetry) measured by the Reprocessed Oximeter pulse oximetry sensors during motion conditions over the range of 70-100% SaO_2 as compared to arterial blood samples assessed by CO-Oximetry. The Accuracy root mean square (ARMS) between measured SpO_2 and reference SaO2 (arterial oxygen saturation) must meet the 3% specification for each Stryker Sustainability Reprocessed pulse oximetry sensor style. Accuracy will be determined by comparing the noninvasive blood oxygen saturation measurement of the pulse oximeter to that obtained from a blood sample and calculating the arithmetic root mean square error (Arms) value. In order to obtain the Arms value, the blood oxygen saturation measurement is subtracted from the pulse oximeter oxygen saturation measurement for a number of samples, the average of this difference is computed as the bias. The standard deviation of the differences is computed as the precision. The square root of the sum of the squares of bias and precision is computed as the Arms Error value. For each range specified, *Sp*O2 ACCURACY of the PULSE OXIMETER EQUIPMENT shall be stated in terms of the root-mean-square (rms) difference between measured values (SpO_{2i}) and reference values (S_{Ri}), as given by the following formula. $A_{rms} = \sqrt{\frac{\sum_{i=1}^{n} (SpO_{2i} - S_{Ri})^2}{n}}$
Eligibility Criteria:	
Ages Eligible for Study: ≥18 and <50 (Adult) Sexes Eligible for Study: All Accepts Healthy Volunteers: Yes	
Inclusion and Exclusion Criteria	Inclusions: • The subject is male or female, aged ≥18 and <50 • The subject is in good general health with no evidence of any medical problems. • The subject is fluent in both written and spoken English • The subject has provided informed consent and is willing to comply with the study procedures

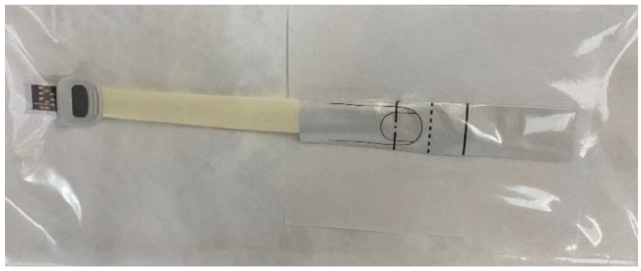
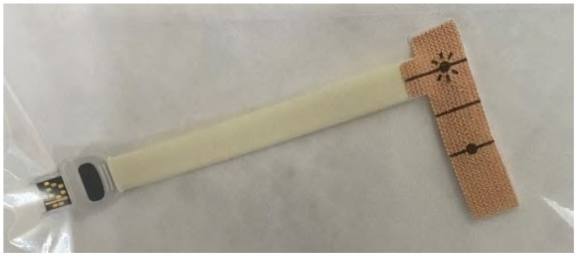
	Exclusions: • The subject is obese (BMI>30) • The subject has a known history of heart disease, lung disease, kidney or liver disease • Diagnosis of asthma, sleep apnea, or use of CPAP • Subject has diabetes • Subject has a clotting disorder • The subject a hemoglobinopathy or history of anemia, per subject report or the first blood sample, that in the opinion of the investigator, would make them unsuitable for study participation • The subject has any other serious systemic illness • The subject is a current smoker • Any injury, deformity, or abnormality at the sensor sites that in the opinion of the investigators would interfere with the sensors working correctly • The subject has a history of fainting or vasovagal response • The subject has a history of sensitivity to local anesthesia • The subject has a diagnosis of Raynaud's disease • The subject has unacceptable collateral circulation based on exam by the investigator (Allen's test) • The subject is pregnant, lactating or trying to get pregnant • The subject is unable or unwilling to provide informed consent, or is unable or unwilling to comply with study procedures • The subject has any other condition, which in the opinion of the investigators would make them unsuitable for the study
Contacts and Locations:	
Locations	United States, California University of California, San Francisco
Sponsors and Collaborators	Stryker Sustainability Solutions, Mike Bernstein (study monitor)
Investigators	Principal Investigator: Dr. Philip E. Bickler, MD, PhD, CA License # is G64031 Co- Principal Investigator: Dr. John R. Feiner, MD

8.0 Product Description

8.1 Intended Use: Reprocessed Masimo RD SET Pulse Oximeter Sensors are indicated for single patient use for continuous noninvasive arterial oxygen saturation and pulse rate monitoring.

8.2 Principle of Operation: The principle of operation of pulse oximetry is based upon the fundamental principle that hemoglobin bound to oxygen (oxyhemoglobin) and hemoglobin unbound to oxygen (deoxyhemoglobin) vary in the absorption of different wavelengths of the light and the absorptions can be used to estimate SpO2 and PR. The mechanism by which this process occurs is the use of red and infrared wavelengths of light delivered by an emitter and the detection of the signal from the light absorption of oxygenated blood and deoxygenated blood to determine functional oxygen saturation of hemoglobin (SpO2).

8.3 Mechanism of Action for Achieving the Intended Effect: The Reprocessed Pulse Oximeter Sensor provides the intended effect equivalent to the previously cleared pulse oximeter sensor in that it utilizes an optical sensor that is applied to the patient's finger or toe through which light is transmitted to the photodetector that detects the signal transmission. The signal transmission is processed by the Pulse Oximeter to provide SpO2 and PR.

Reprocessed Masimo RD SET Pulse Oximeter Sensor 4000 Adt	Reprocessed Masimo RD SET Pulse Oximeter Sensor 4003 Neo
	

9.0 Worst Case Justification

9.1 The pulse oximeter sensors which are identified in Table 1 as subject devices have received FDA clearance for a maximum of four (4) reprocessing cycles. Sensors used in this study were subjected to the maximum number of reprocessing cycles. Catalog number 4000 consists of a non-woven butterfly style tape and catalog number 4003 consists of a woven style tape. There is no worse case model in that the characteristics of both tape types are equivalent within the model family and do not present different challenges during the tape removal process when reprocessing.

10.0 Sample Size Designation

10.1 A typical study will include at least 10 subjects (up to 24 if needed to reach the 200 necessary data points to meet the ISO 80601-2-61:2019). Per FDA guidance, at least 2 or 15% of the subjects will have dark skin pigmentation. Skin pigmentation will be assessed using the Fitzpatrick scale by UCSF study personnel.

10.2 Each study subject will have two reprocessed sensors attached to their fingers. Two Reprocessed Masimo RD SET sensors should be placed on one side of the subject; however, sensors may be placed opposite sides. Digits selected should be two of the three middle fingers on each hand avoiding the thumb or pinky fingers as test sites.

11.0 Preliminary Investigations and Justification of the Study

11.1 Stryker Sustainability Solutions has developed a process to reprocess pulse oximeters that cleans and disinfects the devices active element components and device cord and replaces all patient contacting tapes. The foam covering the cable is cleaned and disinfected but not replaced during reprocessing.

11.2 The manufacturing process for reprocessing includes 100% visual inspection and functional assessment.

11.3 As part of the product development and validation phases of this project, Stryker has performed the following studies:

- Cleaning
- Disinfection
- Biocompatibility
- Performance

12.0 Study Devices

12.1 Device Accountability

12.1.1 Devices will be transported to the test site by the study sponsor.

12.1.2 Use of Study Device

12.1.2.1 Use of devices will be documented electronically as case reports for each subject.

12.2 Packaging and Labeling

12.2.1 Research conducted for this study will utilize investigational devices. The Sponsor is responsible for packaging and labeling of the devices for delivery to the study site. Investigational devices or its immediate package shall bear a label with the following information:

"CAUTION – Investigational device. Limited by Federal (or United States) law to investigational use".

13.0 Procedure

13.1 If the principal investigator deems it necessary, the subject may be asked to run hot water over hands and arms for 5 minutes to improve perfusion. After injection of a local anesthetic, a 22-gauge catheter is inserted in one radial artery. Pulse oximeters are attached to fingers with adequate spacing between fingers or shielding to minimize device cross-talk. Subjects are in a comfortable semi-recumbent position. Subjects then breathe air mixtures containing reduced amounts of oxygen to produce the desired level of hypoxemia. Stable, safe and controlled hypoxia is adjusted manually by an anesthesiologist that permits the inspired gas mixture to be adjusted to achieve a level of lung alveolar gas that will achieve the desired degree of saturation.

13.2 Typically, saturation levels involve one period with air breathing and then at one of three or six levels, e.g. 94%, 90%, 85%, 80%, 75% and 70% or 95%, 85% and 75% saturation. Each level of saturation is held for 30-60 seconds or 60-90 seconds respectively. At appropriate intervals and when oxygen levels are stable, arterial blood samples are obtained from the radial arterial catheter. The operator then changes the inspired oxygen concentration to attain the next desired stead-state level of hypoxia. This study should utilize a three level structure (95%, 85% and 75%). A "run" consists of several stable steady-state hypoxia levels and together takes approximately 20 minutes. Each run is terminated by a breath of 100% O2 followed by room air. Two runs together enable obtaining a total of 20-25 blood samples, 4 samples at each plateau. Saturation of each arterial blood sample is determined by direct oximetry in a Radiometer ABL-90 multi-wavelength oximeter. The precise target levels of saturation can be adjusted to suit the sponsor, but typical testing is done to satisfy ISO and FDA standards for testing, which is 70% to 100%.

13.3 The study takes under 2 hours of each subject's time. Analysis of the data requires several days. Manufacturer's representatives (Stryker) will be present for these tests, and to mount the probes.

14.0 Sponsor Pulse Oximeter Study Data

14.1 Data from test pulse oximeters for comparison to blood values can be obtained in several ways. In every case, the goal is to obtain a reading from the oximeter that corresponds to the associated blood sample or a reference oximeter. Because of circulation delays and instrument averaging time, attempts will be made to create steady state conditions at each level of oxygenation. Therefore, a means should be provided to record the instrument reading at each blood sample. This instrument reading may be obtained with several different approaches. Some instruments have no digital or analog output and the instrument reading may be recorded manually or recorded by a video of the instrument display. Other instruments may have an analog output. The laboratory can record analog data by use of LabView. Digital recording of output can also be

obtained via LabView but this requires information from the sponsor concerning the structure of the digital signal.

14.2 If a manufacturer prefers to collect and analyze the data, the continuous digital signal of each oximeter should be read, for comparison with the blood sample, 9 seconds before the record shows a sudden fall or rise in oxygen saturation, not at the time of blood sampling. This procedure accounts for the delays of finger circulation and uses the estimated delay from the lung to the sample site. There is no useful correlation between the actual time of blood sampling and the oximeter recording because of the variability of tissue blood flow lag. As mentioned, steady-state hypoxia avoids the concern that oximeter reading is not aligned with a blood sample reading.

15.0 Statistics

15.1 The number of subjects and the number of comparisons (paired pulse oximeter readings and arterial saturation values) is determined by current FDA guidance requirements. This is a minimum of 200 data points and 10 subjects. In the course of this type of study, some subjects may drop out, some readings can be lost due to interference and occasionally some do not consent.

15.2 The following demographic data will be collected on the subjects:

15.2.1 Gender (male, female, other)

15.2.2 Age

15.2.3 Skin pigmentation (dark, medium, light) preferably 1-6 using the Fitzpatrick scale

15.2.4 Height (cm)

15.2.5 Weight (kg)

15.2.6 Wrist circumference (cm)

15.2.7 Dominant hand (left or right)

16.0 Data Analysis

16.1 In all cases, the blood analysis data are provided, including the SaO2, MetHb, COHb and Hgb concentration.

16.2 The data analysis report will consist of the following:

16.2.1 A Table of the oximeter readings versus corresponding blood SaO2 values.

16.2.2 Graphic plots of the bias between the oximeter reading and the SaO2 measured by the hemoximeter (on the blood sample, i.e Modified Bland-Altman plots for each instrument or instrument probe combination).

16.2.3 Regression equations for the bias of each instrument.

16.2.4 Tables of the mean error or bias, its standard deviation, standard error, 95% confidence interval, maximum and minimum and root mean square error, all computed both overall and by several sub-ranges of desaturation.

16.2.5 A table of the demographics of the subject population is provided.

17.0 Subject Safety

17.1 Pulse oximeter sensors are typically considered non-significant risk medical devices. The LED light energy utilized in typical test measurements is within the same range as other cleared marketed devices and introduces no further risks. An LED light emits light that passes through the

tissue. A light detector then measures how much light was absorbed by the tissue. Based on the ratio of absorbance of different wavelengths of light, the device calculates the oxygen saturation.

18.0 Risks and Benefits of the Investigational Device and Clinical Investigation

18.1 Breathing a very low oxygen mixture may cause dizziness and might cause loss of consciousness for a few seconds. It may make one feel very short of breath during the test and for a few seconds afterwards. There is a remote possibility that if the subject loses consciousness, he/she might have muscular twitching or convulsions. This study will not seek to reach saturations below 70%. Hypoxia may cause tachycardia and increased blood pressure during the test and might cause headache. In all the years of the lab conducting the study no subject has mentioned headache. Much more severe and prolonged lack of oxygen could cause brain injury or death, but the duration and depth of hypoxia is limited by the test protocol to short intervals. The needle catheter used to take blood may hurt when it is inserted despite the use of local anesthesia, and there may be a black and blue spot afterward. It is remotely possible the artery might be damaged or clot, or a tendon sheath near it be injured by the needle, resulting in some soreness. These risks are unlikely because none of the enrolled 2000+ subjects has ever had a serious complication. Hyperventilating during the part of the study requiring reduced PCO2 may make subjects lightheaded or dizzy. Breathing air with added CO2 may make subjects feel short of breath and cause a headache. Some subjects feel faint when they arrive for the study, apparently related to the thought of having an arterial line. These subjects will likely be excluded from the study.

18.2 Currently the FDA defines pulse oximeters as Class II devices which transmit radiation at a known wavelength(s) through blood and to measure the blood oxygen saturation based on the amount of reflected or scattered radiation and may be used alone or in conjunction with a fiberoptic oximeter catheter. All oximeters being used in this study work by transmittance of radiation at known wavelength(s) through tissue to measure blood oxygen saturation based on the amount of reflected and scattered radiation. The devices under test and this study procedure are considered Non-Significant Risk (NSR).

Non-significant risk letter and checklist were sent to test lab and accepted per a previously approved UCSF IRB for an identical test which can be obtained from UCSF with reference number 330726.

The device and use of the device under test does not meet the definition of a significant risk device. Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

19.0 Invasive Laboratory Testing on Healthy Volunteers

19.1 The risk determination is based on the use of the device in an investigation in addition to the device itself. Generally, the FDA believes pulse oximeters as addressed in the FDA Guidance Document for Pulse Oximeters (March 4, 2013) are non-significant risk devices. Further, the recommendation is to conduct the study in accordance with Clause 201.12.1.101.2 and Annex EE.2 of ISO 80601-2-61:2019, where Annex EE.2 describes the procedure for invasive laboratory testing on healthy volunteers.

20.0 Risk Mitigations

Subjects are all monitored with accurate reference oximeters and continuous end-tidal gas analysis to prevent the risk of more profound hypoxia than desired. Investigators are experienced anesthesiologists adept at assessing breathing and in maintaining appropriate airway conditions. The study room is set up like an OR with all resuscitation equipment immediately available.

21.0 Informed Consent

21.1 Written informed consent is obtained before any study interventions. In discussions with the study coordinator before the day of the study, potential subjects will be offered the consent form to review. On the day of the study subjects are given the consent form which they read and sign if they wish to participate. A study doctor is present to answer questions.

21.2 Only subjects clearly able to understand and read English will be enrolled. Subjects will be asked if they have any questions and are told they can withdraw at any time.

22.0 Investigational Review Board (IRB)/Independent Ethics Committee (IEC)

22.1 Prior to the start of subject enrollment, the investigator will be responsible for obtaining approval from the authorized IRB/IEC for the institution at which the proposed clinical investigation is to be conducted. Written approval from the IRB/IEC should specifically refer to the investigator, the protocol title and date, and subject informed consent date.

22.2 Written IRB/IEC approval and any conditions of approval imposed by the IRB/IEC was obtained by the sponsor/investigator.

22.3 Protocol amendments must also undergo IRB/IEC review and approval at each clinical site. The written approval from the IRB/IEC for the amendment should specifically refer to the investigator, the protocol version number and title, and any amendment numbers that are applicable.

22.4 The IRB approval for this study was obtained May 16th 2023 and is valid through December 19th 2023. Approval reference number 375731.

23.0 Monitoring Arrangements

23.1 A representative from the sponsor and study monitor will provide all monitoring. The Monitor shall be responsible for maintaining a record of the findings, conclusions, and actions taken for the results of monitoring the study ensuring that:

23.2 The monitoring requirements for an NSR device study is identified in 21 CFR 812.2(b) Abbreviated requirements. For monitoring an NSR device investigation, the requirement is to comply with 21 CFR 812.46 with respect to monitoring investigations: (a) Securing Compliance, (b) Unanticipated adverse device effects, (c) Resumption of terminated studies

- Compliance to the signed agreement between the Investigator and sponsor
- The study follows the protocol and any amendments that apply
- Compliance to any conditions of the approval imposed by the IRB or FDA

23.3 Sponsor will assess any new hazards/harms identified during a clinical investigation (i.e., pre- or post-market study) as part of the risk management process per DPCDS-013, Risk Management and the complaint handling process per DP-MCF-001, Division Complaint Handling Process, as applicable.

24.0 Data Storage

24.1 Identifiable subject information is always stored securely following all applicable rules and regulations. Consent forms and other study related documents are retained following UCSF data retentions policy.

25.0 Acceptance Criteria

25.1 The statistical results of the data will be reviewed for the following pass/fail criteria:

25.1.1 At least 200 data points with SpO_2 Accuracy for the range of 70-100%, 3% (A_{RMS}) is considered a Pass per FDA guidance.

25.1.2 At least 10 participants where at least two participants or 15% of participant population will have dark skin pigmentation per the Fitzpatrick scale.

26.0 Protocol Revision History

Revision	Change Order Number	Description
A	ECO153475	Establishment of a new protocol.

27.0 Attachments

27.1 Attachment 1: Non-significant Risk Determination

27.2 Attachment 2: IRB Approval

27.3 Attachment 3: Informed Consent Forms

27.4 Attachment 4: Executed Contract

stryker

Sustainability Solutions

CRD10351

Post-Launch Hypoxia Clinical Study Protocol for Reprocessed Masimo RD SET Pulse Oximeters with motion

Attachment 3

Informed Consent Form

IRB NUMBER: 10-00437
IRB APPROVAL DATE: 02/16/2021
IRB EXPIRATION DATE: 02/15/2022

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: **Accuracy of pulse oximeters with profound hypoxia**

This is a medical research study. Your study doctors, Philip Bickler, MD, John Feiner, MD, Jeffrey Sall, MD, Helge Eilers, MD, Matthew Dudley, MD, Andrew Schober, MD, or Michael Lipnick, MD, from the UCSF Department of Anesthesia and their associates will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to participate in this study because you are healthy, between 18 and 50 years of age and willing to participate in breathing studies with or without blood samples in San Francisco.

Why is this study being done?
The aim of this study is to determine the accuracy of devices called pulse oximeters, which measure blood oxygen by shining light through fingers, ears or other skin, without requiring blood sampling.

How many people will take part in this study?
About 150 volunteer subjects will participate in this study each year.

What will happen if I take part in this research study?
For studies requiring arterial blood sampling by the sponsor, you will have a small plastic tube placed in a wrist artery under local anesthesia. Most studies will require arterial blood sampling, however, some sponsors may choose not to collect blood samples; in these instances, no anesthesia will be used and no arterial catheter will be placed. The study staff will notify you whether this does or does not apply to your particular study date. Standard and test pulse oximeters will be attached to your fingers, forehead, chest, or ears. You will be asked to rapidly breathe in and out of a tube through a mouthpiece, with a nose clip on your nose. The gas you will breathe will be adjusted to lower your blood oxygen saturation from its normal value of 95% - 98% to as low as 70%. The time it will take to desaturate you from your normal blood saturation range to a saturation in the 70s will take about 20 minutes. At most you will be at blood oxygen saturation in the 70s for about 2 minutes.

During studies requiring arterial blood sampling, 20-25 small blood samples (each less than 2 ml or 1 teaspoon) will be taken from the wrist arterial catheter, for a total of less than two ounces of blood. Some sponsors may add additional blood samples for their particular study date; up to 35 samples total may be drawn.

____Please initial here to indicate you have been informed that your study will require additional blood samples (up to 35).

IRB NUMBER: 10-00437
IRB APPROVAL DATE: 02/16/2021
IRB EXPIRATION DATE: 02/15/2022

During some of the testing you may lay flat, or with your head up or down to measure low perfusion. During some of the studies, Testing may also be done with your hand fixed to a motion machine, which rhythmically moves your hand up or down a few inches.

____Please initial here to indicate you have been informed that your study will be examining low perfusion ☐ or motion testing ☐.

During some parts of the testing you may be asked to hyperventilate for a few minutes of to breathe air with slightly increased or decreased amounts of carbon dioxide (CO2).

____Please initial here to indicate you have been informed that your study will require measurements of high or low CO2.

During some of the studies, you may be asked to complete non-invasive experimental 'eye-tracking' tests. Small cameras will track the movement of your eyes throughout the duration of the test.

____Please initial here to indicate you have been informed that your study will be measuring eye-movements during your tests.

During some studies, blood samples may be stored for future analysis. The purpose of this analysis is to investigate the biochemical changes in your blood during hypoxia.

____Please initial here to indicate you have been informed that your study will involve storing your blood samples.

____Please initial here to indicate the sponsor is going to video record your hands and wrist through the study, your face will not be recorded. This video recording will be the property of the sponsor and will usually be kept for one year after the completion of the study.

____Please initial here to indicate that the sponsor will be recording your face through the study. The purpose of recording your face is to determine if blood oxygen saturation can be calculated through minor changes in skin hue at different blood oxygen saturation levels. These recordings will be the property of the sponsor and will be kept for a period of at most 2 years after the completion of the study.

Before you begin the main part of the study…

The following will be done:

- You will answer a few brief questions regarding your general medical history and any smoking habits.
- A partial physical examination may be done of your heart, lungs, heart rate and blood pressure, height and weight.
- We may also test if you have good blood flow in your wrist artery by observing the color of your fingers after making a fist.

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- We will screen you for COVID-19 symptoms. This will include a few brief questions along with a temperature check.

How long will I be in the study?
The study will require you to participate for about 1 hour, on a single day.
Study location: All study procedures will be done at the UCSF Dept of Anesthesiology, on the Parnassus Campus.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. The study doctor may stop you from taking part in this study at any time if he believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

a. Risks of arterial cannulation include bleeding, infection, nerve injury and bruising at the site of catheter insertion. There are also remote risks of an allergic reaction from the lidocaine used for local anesthesia, or the development of arterial spasm, dissection or thrombosis. If the sponsor for your study is not collecting arterial blood samples, this risk does not apply to your participation. You should wait 2 to 3 weeks after arterial cannulation to allow the site to heal before having another arterial line placed in the wrist.

b. The risks of the brief exposures to low oxygen levels include feeling short of breath, headache, and dizziness. Brief loss of consciousness may occur, but is not expected at the levels of oxygen targeted for these tests. If you lose consciousness you may experience slight myoclonic twitching or jerking, this will resolve when you gain consciousness.

c. The risks of hyperventilating include feeling light-headed or dizzy. The risks of breathing air with increased amounts of carbon dioxide include feeling short of breath and developing a headache.

d. For studies requiring eye-tracking, you may experience some watering of your eyes from keeping your eyes open during the test. This can be relieved by blinking.

- **Unknown Risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.
- For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, this study will help develop a medical device that may help others who have low oxygen levels in their blood.

What other choices do I have if I do not take part in this study?

None

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Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include the UCSF Committee on Human Research, the study sponsor and the FDA. The information on your responses to questions about your health will be kept for 6 months and then destroyed.

What are the costs of taking part in this study?

You will not be charged for any of the study activities.

Will I be paid for taking part in this study?

In return for your time, effort and expenses, you will be reimbursed $150 for a 20-sample test, and $200 for a 25-sample test.

If you are participating in a non-blood study, you will be reimbursed $100 for study completion.

For studies requiring additional blood samples, motion evaluations, low perfusion, or high or low carbon dioxide for specific sponsor requests, you may receive an additional $25. The study staff will notify you if this applies to your particular study participation date.

If you do not complete the study, you will be reimbursed $25 per breathing test. A check will be mailed to you approximately 4 weeks after your participation in the study has ended.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctors (Bickler or Feiner) if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at (415) 476-1411.

Treatment and Compensation for Injury:

If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study

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at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor(s) Philip Bickler, M.D. or John Feiner, M.D. at (415) 476-1411

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814**.

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

____Please initial here to indicate you have reviewed the Experimental Subject's Bill of Rights.

____This study has multiple sponsors. The sponsor for this study date has been provided to you. Please initial to acknowledge.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____
Participant (Print name)

_____
Participant's Signature for Consent **Date (mm-dd-yyyy)** **Time (hh:mm)**

_____
Person Obtaining Consent (Print name)

_____
Person Obtaining Consent Signature **Date (mm-dd-yyyy)** **Time (hh:mm)**

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BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,
2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,
4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
5) To be told of the other choices I have and how they may be better or worse than being in the study,
6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
7) To be told what sort of medical treatment is available if any complications arise,
8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,
9) To receive a copy of the signed and dated consent form,
10) To be free of pressure when considering whether I wish to agree to be in the study.

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Committee on Human Research, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the Committee on Human Research, Box 0962, University of California, San Francisco, CA 94143.

Call 476-1814 for information on translations.