Official Title: Noninvasive Hemoglobin Repeatability and Reproducibility in a Blood Donation Setting

Date of Protocol: June 24, 2020

NCT Number: NCT04490863

Noninvasive Hemoglobin Spot Check Repeatability and Reproducibility in a Blood Donation Setting

Sponsor: Masimo
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Principal Investigator: [redacted] MD

Study Device: Rad-67 Pulse CO-Oximeter Device
DCI Mini Sensor

Sponsor Protocol Number: SDBB0005

IRB: Aspire IRB
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Principal Investigator	Title	Signature	Date
[redacted] MD	Principal Investigator		
Sponsor	**Title**	**Signature**	**Date**
[redacted]	Director of Clinical Research		

1 INTRODUCTION

This document is a clinical investigational plan for a human research study sponsored by Masimo Corporation. The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. By participating in the study, the Investigator agrees to adhere to all stipulations of this protocol, the conditions of IRB approval, federal and local regulatory requirements, 21 CFR 812, ISO-14155 and International Conference on Harmonization Good Clinical Practice (ICH GCP) guidance.

To make blood donations, a set of criteria are used to help qualify eligible prospective volunteer donors.[2] One of the criteria prospective donors must meet in order to donate is a minimum hemoglobin concentration to rule out possible anemia. In order to check for the minimum hemoglobin, the center often conducts an invasive test using different methods to determine the potential donor's hemoglobin concentration. In the United States, if the total hemoglobin is <12.5 g/dL for women and <13.0 g/dL for men, the prospective donor is deferred and not allowed to donate.

There is no consensus among blood banks on the best method for qualifying donors based on minimum hemoglobin levels. The international gold-reference standard for quantitative determination of hemoglobin is the hemoglobincyanide (HiCN) method outlined in the Clinical Laboratory Standards Institute.[3] However, this method is complex and not practical for blood donation settings. As a result, hospitals and reference laboratories utilize CO-Oximeters or hematology analyzers to determine hemoglobin concentration.

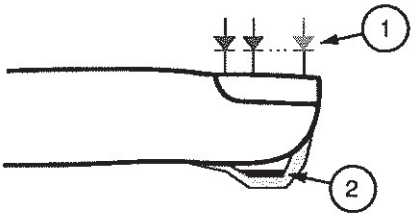
In the past, suitable donors were screened for hemoglobin using the copper sulfate specific gravity method. During the recent years, quantitative methods that measure hematocrit or hemoglobin have been increasingly used with many blood donation centers now using quantitative hemoglobin measurement.[6] The most common test methods used today to screen potential blood donors are point of care analyzers such as the HemoCue, which lyses the red cells, converting the hemoglobin to azide-methemoglobin and quantifying the amount present using spectrophotometry and the microhematocrit, which uses a capillary tube and a high-speed centrifuge. These methods require an invasive capillary blood sample. Some centers still use the copper sulfate method to estimate blood levels and defer those who fail the test. However, not all of these potential donors may truly be anemic[4]. Even mild anemia can be reversed in a short period of time if the necessary advice and treatment is given. Furthermore, these tests are painful for the volunteer, expose the technician to human blood, and require significant training and quality control to ensure appropriate utilization and adherence to CLIA standards.

Masimo has received FDA 510(k) clearance for its noninvasive hemoglobin (SpHb) feature in multiple devices, including the Rad-67, Radical-7 and Pronto for the noninvasive measurement of total hemoglobin (SpHb and Masimo SET measurements of oxygen saturation (SpO2), pulse rate (PR), perfusion index (PI), and respiration rate (RRa)). The SpHb feature analyzes multiple wavelengths of light that pass through the subject's finger to non-invasively provide a hemoglobin concentration reading. SpHb testing has been categorized as CLIA-excluded and requires no user calibration or external quality control procedures[3]. The aim of this study is to evaluate the repeatability and reproducibility of Masimo's pulse CO-oximeter and sensor to determine the device and sensor's precision in SpHb measurements in screening potential blood donors for low hemoglobin levels in a blood donation setting.

1.1 Investigational Devices

The investigational devices to be used in this study are: Rad-67 Pulse CO-Oximeter and rainbow DCI-mini sensor. The Rad-67 device and rainbow DCI-mini sensor are intended for use in clinical and non-clinical settings. The Rad-67 device and DCI-mini sensor have received FDA 510(k) clearance for non-invasive spot-check monitoring of total hemoglobin concentration (SpHb®) for adult patients over the range of 8-17 g/dL. The device's 510(k) clearance does not yet include use of the device for blood donations, thus the Rad-67 and DCI-mini are considered to be investigational devices in this study.

SpHb technology uses a multi-wavelength sensor with various light emitting diodes (LEDs) that pass light through the measurement site to a photodiode (detector) as shown in Figure 1 below. Signal data is obtained by passing various visible and infrared wavelengths through a capillary bed (for example fingertip) and measuring changes in absorption during the blood pulsatile cycle. The detector receives the light and converts it to an electrical signal which is, in turn, used to predict SpHb.



1. Light Emitting Diodes (LEDs) (7 + wavelengths)
2. Detector

Figure 1: SpHb Technology Overview

Investigational devices to be used in this study are: Rad-67 Pulse CO-Oximeter and rainbow DCI-mini sensor. The devices used in this study are manufactured per Good Manufacturing Practice (GMP) with traceability of lot or serial numbers and will be labeled as investigational devices, for clinical research only.

2 STUDY DEVICE

2.1 Description

Investigational Devices:

- Rad-67 CO-Oximeter device
- DCI-mini Sensor

Other Analysis, as applicable:

[redacted]

The Principal Investigator (PI) and delegated study staff will undergo Masimo device training per the Directions for Use prior to performing any study-related procedures. All training will be documented.

2.2 Device Accountability

2.2.1 Receipt of Study Devices

Masimo may ship or hand-carry devices and sensors to the investigative sites. Upon receipt of the of the study device supplies, an inventory must be performed and the Equipment Shipment Check Form [redacted] and the device accountability log will be completed for each device and signed by the receiver. 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. The investigator must notify the study sponsor of any damaged or unusable study devices that were supplied to the investigator's site.

2.2.2 Use of Study Device

Use of devices and sensors will be documented on case report forms (CRF) for each subject. Any unused devices must be returned to the Sponsor at the end of the study or before product expiration date.

2.2.3 Return or Destruction of Study Device

At the completion of the study, there will be a final reconciliation of study devices. 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.

2.3 Risk/Benefits

Benefits: There will be no direct clinical benefits to the enrolled subjects. Future benefits to subjects might include an elimination or reduction in invasive procedures due to the ability to noninvasively measure blood parameters.

Pulse Co-Oximeter risks: The Rad-67 Pulse CO-Oximeter device and the [redacted] device are FDA-cleared and pose no additional risk to the subject.

Sensor risks: The rainbow DCI-mini sensor is FDA-cleared and poses no additional risk to the subject. However, as with all optical sensors, the DCI-mini sensor has the risk of thermal burn. The design includes safeguards, so this risk is believed to be low. All patient-contact materials, including the adhesive when provided, used in the design of the Masimo Rainbow sensors, have been subjected to biocompatibility tests per ISO 10993-1 and results demonstrate that the materials are non-cytotoxic, non-irritating, and non-sensitizing. The sensors have been subjected to performance, mechanical, and electrical testing and results demonstrate that the sensors meet the requirements for safety and effectiveness for the intended use of the product.

[redacted]

3 STUDY OBJECTIVES

The primary objective of this clinical investigation is to report on the repeatability and reproducibility of SpHb measurements from Rad-67 devices and DCI Mini sensors used to screen prospective blood donors at a donation center.

The secondary objective of this clinical investigation is to compare the coefficient of variation (CV) of Rad-67 device to an FDA cleared predicate device for use in a blood donation setting.

4 STUDY DESIGN

4.1 General Design

This is a prospective, nonrandomized study design to investigate the repeatability and reproducibility of SpHb measurements using Rad-67 device and DCI-mini sensors. [redacted]

Measurements will be obtained from individual subjects with replicates while varying devices used and operators, so that variability for between-replicates, between-device, and between-operator may be calculated. A Rad-67 device and the DCI-mini sensor connected are kept as one device unit. [redacted]

[redacted]

4.2 Study Endpoint

The coefficient of variation (CV) will be calculated for both Rad-67 [redacted]. The overall CV for the Rad-67 device should be equal or less than that of the [redacted] device taking into consideration of the standard error of CV.

5 CLINICAL SITE

Site	Site Name and PI	Site Description	Approximate Enrollment
1	[redacted]	Blood donation center	Minimum of 26

6 SUBJECT SELECTION AND WITHDRAWAL

6.1 Population Base

Subjects will be volunteers that are prospective blood donors at least 18 years of age at a blood donation center in the United States. Subjects will be recruited in diversified demographics (age, gender, ethnicity, skin tone, comorbidities, etc.).

6.2 Inclusion Criteria

- At least 18 years of age
- Weight at least 110 pounds
- Subjects with the intention of being screened for eligibility to donate blood
- The subject has given written informed consent to participate in the study

6.3 Exclusion Criteria

- Subjects with skin abnormalities at the planned application sites that may interfere with sensor application, per directions-for-use (DFU) or trans-illumination of the site, such as burns, scar tissue, infections, abnormalities, etc.
- Subjects unwilling to remove nail polish or acrylic nails
- Subjects with blood cancers such as leukemia
- Subjects with hemoglobin disorders such as sickle-cell anemia and thalassemia or with known history of infectious diseases such as HIV/AIDS, syphilis, hepatitis, etc.
- Subjects with self-disclosed/known pregnancy at the time of enrollment
- Subjects deemed not suitable for the study at the discretion of the investigator
- Subjects unlikely to be able to refrain from excessive motion during data collection. Excessive motion includes postural changes, making hand gestures, involuntary muscular movements, etc.

6.4 Subject Recruitment and Screening

Subjects may be recruited for the study from the donation center's research pool, walk-in volunteers, or by advertisement. Information to be disseminated to subjects and any advertisements will be approved by the IRB.

6.5 Early Withdrawal of Subjects

6.5.1 Withdrawal of Individual Subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences or loss of benefits to which they are otherwise entitled. Subjects may be withdrawn from the study prior to expected completion for reasons such as safety concerns, failure to adhere to protocol requirements, subject consent withdrawal, etc.

Any data collected until the time of subject withdrawal will not be included in the final data analysis. Information on the subject's withdrawal should either be documented in the medical record or in the case report forms and should include clear documentation of the reason for withdrawal to the Sponsor.

6.5.2 Follow-up for subjects withdrawn from study

None. There are no long term effects anticipated from participating in this study.

6.5.3 Replacement of individual subjects after withdrawal

In case a subject leaves the study prematurely, another volunteer may be recruited.

7 STUDY PROCEDURES

7.1 Informed Consent and Pre-Screening Procedure

Following identification of a potential eligible subject as defined by the inclusion and exclusion criteria, the subject will be approached by the study staff, who will explain the purpose and procedures of the study in respect to potential risks & benefits, and clarification of subjects' rights & privacy information.

7.1.1 This protocol requires written informed consent, in accordance with applicable federal and state regulations. If the subject expresses interest in participating in the study, he/she will be asked to read the written informed consent.

7.1.2 Once all their questions have been answered and the informed consent signed, they will be enrolled in the study. The point of enrollment is defined as the time at which a patient has signed and dated the consent form.

7.1.3 Subjects must meet all of the inclusion criteria and none of the exclusion criteria in order to participate.

7.1.4 Subject's demographic and general health information (including, but not limited to, age, weight, height, race, ethnicity, skin tone pigmentation [redacted] medical history, smoking habits, and known medical conditions, and vital signs such as blood pressure, temperature, and pulse rate may be recorded on the case report form (CRF).

7.1.5 The Investigator shall retain a copy of the signed informed consent document in each subject's record and provide a copy to the subject. The Investigator shall not allow subjects to participate in the study or consent any subjects prior to receiving IRB approval of the informed consent form.

7.2 General Study Procedures:

7.2.1 Subjects shall be [redacted] n a [redacted] position [redacted].

7.2.2 All study procedures will be performed by trained site staff delegated by the PI.

[redacted]

7.4 Noninvasive Device Measurements:

[redacted] For each subject, [redacted] measurements will be obtained [redacted] Measurements will be taken utilizing the Rad-67 and DCI Mini sensor [redacted]

7.5 Noninvasive Readings using Rad-67 and DCI Mini Sensor:

7.5.1 The best fit finger [redacted] will be selected using a digit gauge. The DCI Mini sensor will then be placed on the appropriate location, per the DFU and/or study procedure manual, and then connected to the Rad-67 pulse CO-oximeter to perform the noninvasive measurement.

[redacted]

[redacted]

7.5.4 At the end of each measurement, all study data will be recorded on the CRF.

[redacted]

7.7 Study Completion

Study completion is defined as when the subject has completed the noninvasive device readings [redacted]. The anticipated duration of subject participation in this study will be approximately 90 minutes. The study enrollment period is expected to be approximately 1-2 weeks.

7.8 Sample Size Determination

[redacted]

7.9 Data Analysis Procedure

7.9.1 The samples collected under this study procedure will be [redacted]

[redacted] Statistical analysis shall be performed on the qualified samples to determine repeatability and reproducibility per CLSI EP05-A3. Calculation methods utilizing advanced analytical methods (e.g. mixed effects modeling) will be used instead of the algebraic formulas in CLSI EP05-A3. [redacted]

7.9.3 The overall Coefficient of Variation (CV) will be calculated as $CV = \frac{100*\sqrt{\text{Reproducibility} + \text{Repeatability}}}{mean(SpHb)}$.

[redacted]

8 SAFETY AND ADVERSE EVENTS

8.1 Definitions

The definitions for adverse event, adverse device effect, serious adverse event, serious adverse device effect, and unanticipated adverse device effect are provided below (ISO 14155:2011, 21 CFR 812.3(s)).

- Adverse Event (AE): an adverse event is any untoward medical occurrence in a subject which need not be related to the device under investigation.
- Adverse Device Effect (ADE): an adverse device effect is any untoward or unintended response to a medical device which may result from insufficiencies in the instructions for use or deployment of the device, or from use error.
- Serious Adverse Event (SAE): a serious adverse event is an adverse event that results in death, inpatient hospitalization, severe or permanent disability, a life threatening illness or injury, fetal distress, fetal death, a congenital abnormality, a birth defect, or medical or surgical intervention to prevent permanent impairment to body or structure.
- Serious Adverse Device Effect (SADE): a serious adverse device effect is an adverse device effect that results in death, inpatient hospitalization, severe or permanent disability or is life threatening.

- Unanticipated Adverse Device Effect (UADE): any serious adverse effect on health or safety or any life threatening problem or death cause by or associated with, a device, if the effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan, or application (including a supplementary plan or application) or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of subjects. Refer to the Device Risk Analysis and Risk Assessment section for details on anticipated adverse device effects.

8.2 Anticipated Adverse Events:

Sensor may cause slight, temporary redness, which should fade away shortly after sensor removal.

Sensor may cause thermal burn; however, the design includes safeguards and this risk is believed to be minimal.

Venous draws may cause swelling, bruising, momentary discomfort at site of blood draw, and in some rare cases lightheadedness, nausea, or fainting.

8.3 Adverse Event Reporting:

- All Adverse Events, both Anticipated and Unanticipated, must be recorded in the within the AE CRF and in the separate Adverse Event Report Form and will follow the site's Adverse Event Policy while also being reported to Sponsor and IRB.
- All Adverse Events must be promptly reported to the Sponsor within 5 business days of when the site first becomes aware of the event.
- All Unanticipated Adverse Device Effects will be also reported to both the Sponsor and the IRB.
- Both Serious Adverse Events and Unanticipated Adverse Device Effects must be reported to the Sponsor within 48 hours.
- All Serious Adverse Events will be also reported to the IRB per IRB reporting requirements. These reports may include, but will not be limited to: date of onset; brief description of the events; their treatment; whether they resulted in death, inpatient hospitalization, severe or permanent disability or were life threatening; their relationship to the study device; and resolution.

8.4 Deviations from the study protocol

Deviations from the protocol must receive both Sponsor and IRB approval before they are initiated with the exception that under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of human subjects may proceed without prior approval of the sponsor or the IRB. Any protocol deviations initiated without Sponsor and IRB approval that may affect the scientific soundness of the study, or affect the rights, safety, or welfare of study subjects, must be documented and reported to the Sponsor and to the IRB as soon as a possible, but no later than 5 working days of the protocol deviation. If protocol deviations continue to occur frequently at a study site, a corrective and preventive action (CAPA) may be opened by the Sponsor.

8.5 Withdrawal of IRB approval

An investigator shall report to the sponsor a withdrawal of approval by the investigator's reviewing IRB as soon as a possible, but no later than 5 working days of the IRB notification of withdrawal of approval.

9 VULNERABLE POPULATIONS

9.1 Definition

9.1.1 Vulnerable populations are defined as disadvantaged sub-segment of the community requiring utmost care, special considerations and protections in research. This study may recruit subjects from the following: economically disadvantaged or unemployed, educationally disadvantaged, limited English skills and/or Non-US citizens, employees/colleagues of the Principal Investigator and/or study staff.

9.2 Protection of vulnerable subjects

- The same compensation will be provided for all study participants, including 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.
- If subjects are employees, colleagues, or students of the Investigator and/or study staff, the IRB will add non-coercion language to the informed consent form and Investigator will explain that participation does not affect subject's employment, benefits, or position at the company and cannot be the grounds for termination. Likewise, if employees refuse to participate or withdraw from the study, their employment, benefits, and position at the company will in no way be affected.
- Medical care will be provided to these subjects after the clinical investigation has been completed if they are injured as a direct result of participating in this research study. The cost of treatment for any research related injury will be covered by Masimo.

9.3 Responsible Parties

- The IRB will review research with vulnerable populations and evaluate consent, level of risk, coercion, and the reason for choosing this particular subject population. The IRB will be responsible for determining what practices will include continuing review for compliance while monitoring these studies.
- The Investigator holds the ultimate responsibility for protecting the rights, safety, and welfare of research subjects by ensuring that all regulations and proper documentation of consent is handled in a compliant and timely manner.

10 DATA MANAGEMENT

10.1 Confidentiality of Records

Information about the patients will be kept confidential. The data will be stored on a password protected database on a secure server, accessible only to the Investigators. 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, finger location of the sensor, and the recordings from the pulse oximeter.

10.2 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, recorded data from automated instruments, and copies or transcriptions certified after verification as being accurate and complete. For this study, the case report forms may also be used as source worksheets.

10.3 Case Report Forms

Paper or electronic Case Report Forms (CRFs) may be utilized in this study. The site shall capture study data on the CRFs for each subject enrolled. The CRFs will be completed, signed and dated by the PI or delegated personnel. This also applies to those subjects who fail to complete the study. If a subject withdraws from the study, the reason must be noted on the CRF. Case report forms are to be completed on an ongoing basis. CRF entries and corrections will only be performed by study site staff, authorized by the investigator. Entries and corrections to the CRF will be made following Good Documentation Practices (GDP).

The CRF will include the following information, including but not limited to: inclusion/exclusion criteria, whether subject consent was obtained before start of study, demographic information, device readings, and if occurrence of any adverse event, protocol deviation, and device deficiencies, etc. The CRFs will be signed by the PI to attest that the data are complete and accurate. A copy of paper CRFs shall be provided to Masimo.

CRF entries will be verified by study monitor and any errors or inconsistencies will be queried to the site on an ongoing basis. Any changes made within an electronic CRF will be tracked by audit trail. Any changes on a paper CRF will be made directly on the CRF and will be initialed and dated by the person making the change. Query resolution will be assessed and confirmed by study monitor during site visit.

10.4 Data Transfer and Storage

10.4.1 Training on CRF completion will be provided to study personnel prior to data collection.

10.4.2 If paper CRFs are used, original CRFs will be scanned and sent to sponsor, then stored in a secure location at the site.

10.4.3 Only authorized sponsor personnel will have access to study data, and will move it to a secure and backed-up drive at Masimo.

10.4.4 CRFs will be checked for accuracy and completeness of data. If there are inconsistent or missing data points, a query list will be generated and submitted to the PI or designee. Masimo engineers are notified that data are ready for analysis. To ensure data integrity, Masimo engineers will only have read access to study data and therefore, are unable to unintentionally tamper with the original data files.

10.5 Record Retention

All study information, including but not limited to study correspondence, study logs, device accountability records, consent forms, subject records, and copies of CRFs should be maintained in the Investigator site files.

Study records shall be retained during the study and for a minimum of two years after date of study closure or date when records are not required to support 510(k) clearance. The Institution's own retention policies and regulations may apply in addition to the minimal requirement.

The Sponsor is responsible for verifying study data, retaining records, analyzing data, and authoring study reports.

11 MONITORING PLAN

11.1 As the Sponsor of this clinical investigation, Masimo Corporation is required by 21 CFR, Part 812, of the Food and Drug Administration regulations to monitor and oversee the progress of the investigation. The monitor(s) assigned by Masimo Corporation to this task will be trained on departmental SOPs on conduct and monitoring of sponsored studies.

11.2 In accordance with Good Clinical Practices (GCP) guidelines, there will be at least three scheduled monitoring visits to ensure overall regulatory compliance of the study:

- An initiation visit, prior to any subject enrollment to confirm site readiness, and to document training on the study protocol and procedures, and use of equipment.
- At least one interim monitoring visit during the initial round of data collection and at least one visit 4-6 weeks after data collection is complete.
- A final close out visit after the last subject has completed the study.
- NOTE DURING COVID-19 PANDEMIC: Monitoring activities may be modified or postponed until such a time that restrictions prohibiting travel and hospital access are lifted.

11.3 The Investigator shall allow access to all source documents needed to verify the entries in the CRFs and other GCP-related documents (IRB approvals, IRB correspondences, and ICFs) provided that subject confidentiality is maintained in agreement with HIPAA regulations.

11.4 It will be the monitor's responsibility to inspect the CRFs at regular intervals throughout the study, to verify the adherence to the CIP and the completeness, consistency and accuracy of the data being entered on them.

11.5 During each visit, the monitor will also verify presence of informed consent, adherence to the inclusion/exclusion criteria, and documentation of SAEs/SADEs and protocol deviations/violations, and check CRF against medical records and real-time data stored within the Rad-67 device.

11.6 After each visit, the monitor will provide a monitoring follow-up letter to the investigator within 4 weeks of visit completion. The follow-up will detail findings and open action items observed during the visit. It is the responsibility of the Principal Investigator and Study Coordinator(s) to respond to the findings of the monitoring report, and complete any open action items as soon as possible but no later than 60 days of receiving the monitoring report. Any open action items not completed within the time allowed may be sufficient grounds for study site suspension or termination; it will be up to the sponsor to determine whether any incomplete action items are sufficient grounds for suspension or termination. See Section 16 for details on suspension and termination.

11.7 Depending on the quality of the data and/or changes to factors affecting subject safety, additional monitoring visits may be necessary according at the sponsor's discretion.

11.8 The Investigator will provide the monitor access to all necessary records to ensure the integrity of the data (21 CFR 812).

12 ADMINISTRATIVE ASPECTS

12.1 Protection of Human Subjects

Per 21 CFR 50, written consent must be obtained from each subject or from their legal guardian prior to any study procedures in accordance with applicable federal, state, and study site regulations. The Investigator must keep a copy of the signed consent form in each subject's record and provide a copy to the subject as well. The Investigator shall not allow a subject to participate in a study or sign consent prior to IRB approval.

Prior to the start of data collection or subject enrollment, the Investigator must provide documentation of IRB approval of the study protocol and a copy of the approved informed consent form (21 CFR 50).

12.2 Institutional Review Boards

The Sponsor and/or Investigator must submit the protocol to the appropriate IRB and obtain a copy of the written and dated approval letter.

The approval letter should state the name of the documents reviewed, date of review, date of approval, and reference the study name (protocol title, study number, and version).

The informed consent used by the Investigator must be reviewed and approved by the Sponsor prior to submission to the IRB. The Investigator cannot enroll subjects until a copy of the approved informed consent is obtained from the IRB.

Any amendments to the protocol or informed consent should be submitted to the IRB for review and approval per 21 CFR 56. The IRB should be notified of any changes that may affect conduct of the study or pose safety risks to the subjects.

12.3 Confidentiality

All data collected will be kept confidential and de-identified. It can only be accessed by researchers and will be used for research purposes only.

12.4 Protocol Amendments

Any changes made to the clinical investigational plan/study protocol will be documented by way of an amendment. Before submitting protocol amendment to the IRB for approval, the protocol amendment must be agreed upon and signed by both the Investigator and the Sponsor. The Investigator shall not make any changes to the protocol without Sponsor approval and documented approval from the IRB. Both PI and Sponsor will retain the IRB approval letter and approved protocol as confirmation that the protocol amendment was approved.

12.5 Suspension or Termination of Study Site

The Sponsor can suspend or prematurely terminate the PI's and study site's participation in the study, particularly if Sponsor finds serious non-compliance by the PI or site, and if such non-compliance was not resolved in a timely manner. The Sponsor will document the decision to suspend or terminate the investigation in writing. A suspended study site cannot enroll new subjects.

If the Sponsor determines that the study site's compliance to GCP and federal regulations to be inadequate at any point during the study, and Sponsor moves to suspend or terminate the study site, the Sponsor will provide notification in writing to the principal investigator and IRB as necessary. The study site is eligible for reinstatement upon correction of any findings and any open action items prior to the suspension, and provides a written guarantee that the same non-compliance will not reoccur in the future. Site can only resume subject enrollment upon receiving written notification of reinstatement from the Sponsor and/or IRB.

12.6 Termination of Clinical Investigation/Study due to UADE

The clinical investigation may be terminated if Sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to the subjects. Termination shall occur not later than 5 working days after the Sponsor makes this determination, and not later than 15 working days after the Sponsor first received notice of the effect.

The Sponsor may resume the terminated clinical investigation with prior IRB approval if the device is non-significant risk.

13 AGREEMENT BETWEEN INVESTIGATOR AND SPONSOR REGARDING RESPONSIBILITIES FOR GOOD CLINICAL PRACTICE

International Conference of Harmonization (ICH) E6 Good Clinical Practice guidance is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.

It specifies general requirements intended to:

- Protect the rights, safety and well-being of human subjects,
- Ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- Assist Sponsors, monitors, Investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

The Principal Investigator of the clinical investigation shall:

- Obtain and maintain IRB approval of the study.
- Ensure all subjects are consented prior to enrollment, per FDA Code of Federal Regulations titled 21 CFR 50.
- Conduct the clinical investigation in accordance with the protocol, all applicable laws and federal regulations, and conditions or restrictions implemented by the governing IRB.
- Ensure only appropriately trained personnel will be involved in clinical investigation.

- Maintain study records mentioned in the CIP.
- Maintain logs for study team delegation, site visit/monitoring, equipment disposition, study team training, subject recruitment and enrollment.
- Evaluate all adverse events and adverse device effects and determining whether the study is safe to continue.
- Allow the Sponsor to conduct periodic monitoring of study activities to ensure GCP compliance.
- Not promote device prior to clearance by FDA for commercial distribution, except for academic purposes and scientific presentations.

The Sponsor shall ensure existence and record of all necessary compliance documents, and will conduct monitoring visits to ensure appropriate conduct of the study.

14 REVISION HISTORY:

Version Number	Version Date	Summary of Revisions Made:
1.0	18Jun2020	Original version

15 REFERENCES

1. WHO 2010. Towards 100 % voluntary blood donation: a global framework for action. Geneva: WHO Press.
2. Sundar P, Sangeetha SK, Seema DM, Marimuthu P, Shivanna N. *Pre-donation deferral of blood donors in South Indian set-up: An analysis*. Asian J Transfus Sci. 2010; 4(2):112–5.CMS transmittal #1912. Healthcare Common Procedure Coding System (HCPCS) Codes Subject to and Excluded from Clinical Laboratory Improvement Amendments (CLIA) Edits, change request #6812. Department of Health and Human Services, February 5, 2010.
3. CLINICAL LABORATORY STANDARDS INSTITUTE (CLSI)

EP09A2 IR	Method Comparison and Bias Estimation Using Patient Samples
H1-A4	Evacuated Tubes and Additives for Blood Specimen Collection – Forth Edition; Approved Standard
H3-A4	Procedure for the Collection of Diagnostic blood Specimens by Venipuncture; Approved Standard – Fourth Edition
H4-A4	Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture Approved Standard – Fourth Edition
H15-A3	Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood; Approved Standard – Third Edition
H18-A2	Procedures of the Handling and Processing of Blood Specimens; Approved Guideline – Second Edition
H18-A4	CLSI Hematology Guidelines. "Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests."

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