CLINIMARK Test Plan
Respiratory Rate Verification Study - Gabi SmartCare Gabi Band
PR 2022-495

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Document Ownership: Document is in accordance with Code of Federal Regulations for Non-Significant Risk Investigations and ISO 14155:2011 where applicable

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STUDY PROCEDURE:

Respiratory Rate Verification Study – Gabi SmartCare Gabi Band
Clinimark Study ID# PR 2022-495

COMMERCIAL SPONSOR:

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Clinimark Statements

Confidentiality

The information contained in this document is confidential and is intended for the use of clinical investigators. It will not be copied by or distributed to persons not involved in the clinical investigations of Gabi SmartCare, unless such persons are bound by a confidentiality agreement with Clinimark or Gabi SmartCare.

Impartiality

Clinimark is committed to maintaining impartiality of laboratory and study activities. Personnel are trained on processes and protocols are followed to ensure conformity of the activities. Commercial, financial and other pressures are not allowed to compromise the impartiality of laboratory activities. This includes those risks that arise from lab activities, lab relationships, or from the relationships of its personnel.

The risk of Impartiality is mitigated by conducting this study according to the mutually agreed upon protocol, contractual arrangements, and standards or guidance documents if applicable.

Glossary

- **CIP** - Clinical Investigation Plan
- **FDA** – Food and Drug Administration
- **IRB** – Independent Review Board
- **ISO** – the International Organization for Standardization
- **NIST** – National Institute of Standards and Technology, **NIST** is the federal technology agency that works with industry to develop and apply technology, measurements, and standards.
- **Reference** – established accuracy used for clinical evaluations of other instruments
- **Device Under Test (DUT)** – the device being clinically evaluated
- **NSR** – Non Significant Risk
- **PPG** - Photoplethysmography
- **bpm** – beats per minute, in regards to heart or pulse rate
- **BPM**– Breaths per minute, in regards to respiratory rate
- **$EtCO_2$** – End Tidal Carbon Dioxide
- **RR** – Respiration/Respiratory Rate
- **PR** – Pulse Rate
- **ROI** – Region of Interest
- **A_{RMS}** - Accuracy Root Mean Square

$$Arms = \sqrt{\frac{\sum_{i=1}^{n}(DUT_i - \mathrm{Re}f_i)^2}{n}}$$

Where:

- A_{RMS} is the accuracy root mean square.
- DUT is the test device during sample i.
- Ref is the Reference Respiratory Rate ($EtCO_2$) during sample i.
- n is the number of points.

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Summary

Objectives of the Clinical Investigation Plan

The purpose of this study is to conduct a Respiratory Rate accuracy Verification comparing the Gabi SmartCare Gabi Band to the Reference, an FDA cleared End Tidal Carbon Dioxide monitor (GE Datex-Ohmeda).

The testing will be conducted in order to obtain a full data set for Verification on a minimum of 23 participants. Multiple developmental phases may be conducted and will be reviewed for readiness for continuation to Verification. If modifications are warranted, the initial data sets will be used for algorithm development. The study will be split up into two phases:

- Phase I with a minimum of 8 subjects
- Phase II with a minimum of 15 subjects

Background

Respiratory Rate is an important physiological measurement in the healthcare setting. The gold standard in Respiratory Rate is based off of an airway measurement using end tidal carbon dioxide ($EtCO_2$) respiratory rate.

The medical device studied under this protocol will be the non-invasive and investigational Gabi SmartCare Gabi Band. All appropriate preliminary testing on the Gabi SmartCare Gabi Band has been successfully performed and demonstrates safety and efficacy for use in human studies prior to Clinimark's receipt of the devices. Gabi SmartCare Gabi Band is a non-invasive device that allows for real-time, remote monitoring using a sensor applied on the participant's upper arm.

Protocol Overview

After IRB approval, a minimum of 23 volunteer test participants will be enrolled for the verification study population. A maximum of 60 participants will be enrolled. An attempt will be made to include 3 darkly pigmented participants or 15% of the participant pool (whichever is larger). Participants will be from 0-5 years of age with the following distribution:

Population	Age Population	Requirement
Neonates	0-28 days	No requirement
Infant	>1 month – 24 months	Minimum 30% of participants
Pediatrics	>2 years – 5 years	Minimum 30% of participants

Each participant is expected to take 1-2 hours, including paperwork, sensor application, and a maximum of 60 minutes of data collection. Each participant will be connected to a commonly used End Tidal Carbon Dioxide monitor (GE Datex-Ohmeda) and the Gabi SmartCare Gabi Band. The end tidal carbon dioxide ($EtCO_2$) monitor will determine performance of respiratory rate metrics (GE Healthcare S5 Compact Monitor with M-COVX (K001814) or E-CaiO (K051092) modules). Each participant will be instrumented with neonatal or pediatric nasal cannula that allows for measurement of the $EtCO_2$. SpO_2 sensors may be placed on the feet and/or toes for safety monitoring purposes.

Data will be simultaneously and continuously recorded from the Reference $EtCO_2$ monitor and the Device Under Test (DUT). Periods of quiet will be encouraged. Data will be marked for stable quiet periods that are useable for analysis. There is no additional follow-up required for the investigation.

One minute epochs will be generated from the stable data periods for analysis. For verification, the Reference $EtCO_2$ waveform will be scored by counting the respiratory peaks per minute (See Appendix B: Sample Waveform

Scoring Form for an example). The reviewers counting the raw $EtCO_2$ waveform will be blinded to the results from the test device. The DUT data will be averaged over the corresponding one minute period. The Accuracy root-mean-square (A_{rms}) will be the basis for evaluation and acceptance.

To 'Pass' this test the Gabi SmartCare Gabi Band (Device Under Test) must demonstrate an Accuracy root-mean-square (A_{rms}) of ≤3.0 breaths per minute when compared to the Reference $EtCO_2$ monitor.

Study Population

The study population will include a minimum of 23 neonates, infants, and pediatrics from 0-12 years of age. A maximum of 60 participants will be enrolled. The participant selection will be an equitable distribution of males and females of any race with varying skin tones. An attempt will be made to include 3 darkly pigmented participants (Fitzpatrick 5 or 6) or 15% of the participant pool (whichever is larger).

The parents or guardian of the participants must understand the study and consent to their child's participation in the study by signing the Informed Consent Form. Subjects 7 to 12 years of age will be provided an Assent. The study will be explained within his/her ability to understand. Participant enrollment and participation in this clinical study is based on meeting the inclusion criteria and none of the exclusion criteria, a satisfactory screening, and the participant and data demographics needed for the study.

Inclusion Criteria

- Ability of the parent or guardian to understand and provide written informed consent
- Participant is 0 to 12 years of age
- Subjects that are between 7 and 12 years of age must provide Assent to participate in the study

Population Criteria to be Included

- A minimum of 30% of participants will be >1 month to 24 months old
- A minimum of 30% of participants will be >2 years to 12 year

Exclusion Criteria

- Participants evaluated by the Investigator and Clinical Staff and found to be medically unsuitable or have self-reported health conditions that are currently unstable as identified in the Participant Demographics and Screening Record Form
- Participant has injuries, deformities or abnormalities that may prevent proper application of the device under test
- Participants with severe contact allergies to standard adhesives, latex or other materials found in pulse oximetry sensors, ECG electrodes, or other medical sensors (self-reported)

It is expected that the data collection will take two days for Phase I and four days for Phase II. There is no additional follow-up required for the investigation.

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Objectives of the Clinical Investigation Plan

The purpose of this study is to conduct a Respiratory Rate accuracy Verification study comparing the Gabi SmartCare Gabi Band to the Reference, an FDA cleared End Tidal Carbon Dioxide monitor (GE Datex-Ohmeda).

The testing will be conducted in order to obtain a full data set for Verification on a minimum of 23 participants. Multiple developmental phases may be conducted and will be reviewed for readiness for continuation to Verification. If modifications are warranted, the initial data sets will be used for algorithm development. The full Verification set will be collected independent of developmental data sets. The study will be split up into two phases:

- Phase I with a minimum of 8 subjects
- Phase II with a minimum of 15 subjects

Identification and Description of the Investigational Device

The Gabi device consists of a sensor head with an attached armband to make the wearable device. The sensor head contains a photoplethysmography sensor (PPG) and all other electronics. The PPG sensor is seated on the underside of the sensor head to maintain skin contact. All data is stored on the collection tablet and uploaded to the Gabi Cloud for analysis when data collection is stopped.

Figure 1: The Gabi SmartCare Gabi Band – The Device Under Test

The intended purpose of the Device Under Test is continuous, non-invasive monitoring on the neonatal, infant, and pediatric populations. For this evaluation, the device will be run in a continuous data collection mode. The accompanying acquisition software will be provided by Gabi SmartCare.

The Gabi SmartCare Gabi Band are investigational and has not been cleared by the FDA. The sensor and the arm band are the components expected to come in contact with the participants.

Instructions for use, storage and handling can be found in the Device Operator's Manual. Device model numbers, software version, serial numbers, date(s) of use, and participant ID number(s) will be recorded on the Case Report Forms.

All appropriate testing to demonstrate safety for use in human studies prior to Clinimark's receipt of the device was completed. Such documentation will reside in the design history files of the Sponsor. Documentation will be provided regarding the safety of the investigational device.

Data Acquisition System for the Investigational Device

The data from the investigational devices/smartphone will be collected by a trained member of Clinimark, separate from the Clinimark automated data collection system.

Safety Equipment

Patient monitor(s) used during the study to observe a participant's vital signs including SpO2, pulse rate, respiratory rate, end-tidal CO_2 with capnograph:

- SpO_2 monitoring - GE Healthcare S5 Compact Monitor with M-NESTPR (K993608) or E-PRESTN (K031781) module, and/or other Multi-parameter monitor, GE Healthcare (Datex-Ohmeda) 3900 TruTrak+, GE Healthcare S5 Compact Monitor with M-NESTPR (K993608) or E-PRESTN (K031781) module, and/or Nellcor N600x Pulse Oximeter
- $EtCO_2$ Capnography / Respiratory Rate - GE Healthcare S5 Compact Monitor with M-COVX (K001814) or E-CaiO (K051092) modules
- Portable oxygen tank, mask and ambu bag
- Blood pressure cuff and stethoscope

Preliminary Investigations and Justifications of the Study

Gabi SmartCare is dedicated to developing and applying innovative electronic medical solutions that improve patient care in multiple clinical settings. As part of the product development, Gabi SmartCare retained the services of Clinimark, LLC to conduct a respiratory rate accuracy study.

Studies previously conducted at Clinimark:

- Clinimark Study ID# PR 2022-477 "SpO2 Verification and Optional Calibration Study"

Risks and Benefits of the Investigational Device and Clinical Investigation

The devices under test in this study are considered non-significant risk devices. The device and use of the device under test does not meet the definition of significant risk device under 21 CFR 812.3(m)

For the purpose of this study:

- It is not intended as an implant.
    - Sensors are applied to the surface of the area and is removed following data collection typically less than 1 day.
- It is not purported or represented to be for use in supporting or sustaining human life, nor does it present a potential for serious risk to the health, safety, or welfare of a participant.
    - Monitors are not used to support or sustain human life.
- It is not for use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health
    - Monitors are Class II devices used to measure respiratory rate. They are not used to diagnose, cure, mitigate, or treat disease. These devices are typically labeled with a general indication for non-invasive measurement of respiratory rate.
- The device as used in this investigation does not present a serious risk to the health, safety, or welfare of a participant.
    - See below for discussion of risk associated with the device and use of the device.

There are no anticipated risks or adverse device effects to be assessed. There are no contraindications for use in the proposed study / study population. There may be other risks to the participant associated with the device or procedure that are unforeseeable at this time.

Sensors

Sensor placement involves positioning sensors on volunteer participant in the same manner that is used on hospitalized patients. The sensors may be warm to the touch. Under normal operating conditions, no fault conditions, the sensors are not expected to overheat. If the sensors are too warm, they will be removed immediately. Adhesive sensors or tape may cause some irritations to the skin in some participants. Every effort will be made to minimize products with natural rubber or latex. Products containing natural rubber or latex will be identified. The risk in the use of the sensor is believed to be minimal.

Nasal Cannula

The nasal cannula are made of soft, flexible plastic so as to minimize the discomfort level as much as is reasonably possible. Materials may cause some skin irritations. Insertion and removal of a nasal cannula may cause nasal irritation, discomfort, or pain.

General Electrical Hazards

Electrical hazards are a potential risk with all electrical equipment. The equipment used in this study has been designed to meet applicable safety standards. The equipment will be safety and functionally tested prior to participant use. The possibility of any electrical hazard is extremely remote.

Benefits

The benefits to the study are to the advancement of non-invasive medical monitoring of patients by improving accuracy and performance of the monitors. There are no direct benefits to the participants involvement in this study other than being a paid volunteer. The only alternative to this study is to NOT participate.

Design of the Clinical Investigation

Method

The purpose of this study is to conduct a Respiratory Rate accuracy Verification comparing the Gabi SmartCare Gabi Band to the Reference, an FDA cleared End Tidal Carbon Dioxide monitor (GE Datex-Ohmeda).

This study is a comparative, single-center, non-randomized study in a minimum of 23 participants for the verification. Each participant test is expected to take approximately 1-2 hours. Typically, up to 4 participants will be run per day. It is expected that the data collection will take two days for Phase II and four days for Phase II. A maximum of 60 participants will be enrolled. An attempt will be made to include 3 darkly pigmented participants (Fitzpatrick of 5 or 6)or 15% of the participant pool (whichever is larger). Participants will be from 0-12 years of age with the following distribution:

Population	Age Population	Requirement
Neonates	0-28 Days	No requirement
Infant	>1 month – 24 months	Minimum 30% of participants
Pediatrics	>2 years – 12 years	Minimum 30% of participants

The parent or guardian will be provided an IRB approved Informed Consent. As applicable, parent or guardian will be told about any new information that might change their decision to participate. Participants whose parent or guardian have completed the informed consent, completed the Participant Demographics and Screening Record Form, and met inclusion criteria and none of the exclusion criteria will be enrolled in the study. Participants ranging in age 7–12 years will additionally go through an Assent process.

Each participant will be connected to a commonly used End Tidal Carbon Dioxide monitor (GE Datex-Ohmeda) and the Gabi SmartCare Gabi Band. The end tidal carbon dioxide ($EtCO_2$) monitor will determine performance of respiratory rate metrics (GE Healthcare S5 Compact Monitor with M-COVX (K001814) or E-CaiO (K051092) modules). Each participant will be instrumented with neonatal or pediatric nasal cannula that allows for measurement of the $EtCO_2$. SpO_2 sensors may be placed on the feet and/or toes for safety monitoring purposes.

Data will be simultaneously and continuously recorded from the Reference $EtCO_2$ monitor and the Device Under Test (DUT). Periods of quiet will be encouraged. Data will be marked for stable quiet periods that are useable for analysis. There is no additional follow-up required for the investigation.

One minute epochs will be generated from the stable data periods for analysis. For verification, the Reference $EtCO_2$ waveform will be scored by counting the respiratory peaks per minute (See Appendix B: Sample Waveform Scoring Form for an example). The reviewers counting the raw $EtCO_2$ waveform will be blinded to the results from the test device. The DUT data will be averaged over the corresponding one minute period. The Accuracy root-mean-square (A_{rms}) will be the basis for evaluation and acceptance.

To 'Pass' this test the Gabi SmartCare Gabi Band (Device Under Test) must demonstrate a respiratory rate Accuracy root-mean-square (A_{rms}) of ≤3.0 breaths per minute when compared to the Reference $EtCO_2$ monitor.

Video and/or Photos

In this study photographs or video may be taken of the sensor application sites during sensor application for data collection purposes and the Study Sponsor's internal research and development purposes only. This allows the sponsor to analyze the data and observe sensor placement. Pictures may be taken of any site where we have placed equipment. The study equipment will be photographed, however, in some circumstances it may be unavoidable to not photograph the participant's face. In order to protect the participant's identity, the name will be kept confidential at all times.

Equipment

The MediCollector software will be used to collect the reference data.

Description of MediCollector

- Computer with data collection software, able to stream data as it is recorded with the ability to add annotations
- Direct cable connection with the Datex-Ohmeda S/5 Multi-parameter Monitor
- Collects a variety of signals including values displayed by the S5 as well as the raw waveforms
    - Up to 8 signals can be collected

MediCollector –Signal Channels Examples				
#	Name	Description	Freq. of Collection (Hz)	Units
1	CO_RR	Respiratory Rate	0.2	breaths/min
2	CO2	CO_2 Concentration (RR waveform)	25	%

Safety Equipment

- GE Healthcare Datex-Ohmeda S/5 Multi-parameter Monitor, M-NESTPR (K993608) or E-PRESTN (K031781) module with SpO_2, GE Healthcare (Datex-Ohmeda) 3900 TruTrak+ (K021955) and/or Nellcor N600x Pulse Oximeter (K123581) with appropriate neonatal, infant, or pediatric sensors
- Portable oxygen tank, mask and ambu bag

Supplies for Participant

- Neonate or pediatric nasal cannula for $EtCO_2$ measurement

Reference

- GE Healthcare Datex-Ohmeda S/5 Multi-parameter Monitor, M-COVX (K001814) or E-CaiO (K051092) module (Reference $EtCO_2$)

Investigational Device

- Gabi SmartCare Gabi Band (DUT)
- Computer, tablet, or phone for data capture transfer

There are no deviations expected from this investigation plan. Should deviations be needed, discussions will be conducted with Gabi SmartCare, Principal investigator, and reported to the IRB per the reviewing IRB guidelines.

Study Population

The study population will include a minimum of 23 neonates, infants, and pediatrics from 0-12 years of age. A maximum of 60 participants will be enrolled. The participant selection will be an equitable distribution of males and females of any race with varying skin tones. An attempt will be made to include 3 darkly pigmented participants (Fitzpatrick 5 or 6) or 15% of the participant pool (whichever is larger).

The parents of the participants must understand the study and consent to their child's participation in the study by signing the Informed Consent Form. Subjects 7 to 12 years of age will be provided an Assent. The study will be explained within his/her ability to understand. Participant enrollment and participation in this clinical study is based on meeting the inclusion criteria and none of the exclusion criteria, a satisfactory screening, and the participant and data demographics needed for the study.

Inclusion Criteria

- Ability of the parent or guardian to understand and provide written informed consent
- Participant is 0 to 12 years of age
- Subjects that are between 7 and 12 years of age must provide Assent to participate in the study

Population Criteria to be Included

- A minimum of 30% of participants will be >1 month to 24 months old
- A minimum of 30% of participants will be >2 years to 12 year

Exclusion Criteria

- Participants evaluated by the Investigator and Clinical Staff and found to be medically unsuitable or have self-reported health conditions that are currently unstable as identified in the Participant Demographics and Screening Record Form
- Participant has injuries, deformities or abnormalities that may prevent proper application of the device under test
- Participants with severe contact allergies to standard adhesives, latex or other materials found in pulse oximetry sensors, ECG electrodes, or other medical sensors (self-reported)

Fitzpatrick Scale

The Fitzpatrick scale will be used to access skin tone. The following chart will be used:

Figure 2: The Fitzpatrick Scale

Duration of Clinical Investigation

Each participant test is expected to take approximately 1 – 2 hours. Typically, four participants will be run per day. It is expected that the data collection will take 5 to 7 days for verification. There is no additional follow-up required for the investigation.

Criteria for Study Termination

The study will be terminated if any of the following conditions occurs:

- Study is complete
- The participant's parent or guardian may stop the study for any reason without prejudice
- Withdrawal by Sub-Investigator / Investigator
- Study Stopped due to Technical Problems
- Study may be stopped due to Protocol Deviation
- Study Terminated by Sponsor
- Study Stopped due to Adverse Event

Any data collected to the point of a decision to terminate the study will be reviewed for inclusion to the analysis prior to generation of the final results. Data excluded from the analysis will be documented with justifications for the Verification of the product. During the development phase, usage and removal of the data is at the sponsors discretion.

Procedure

1. Complete equipment setup and checkout prior to starting study.
2. Set and / or synchronize the computer clocks for the sponsor and Clinimark data collection systems
3. Explain the procedure to the participant's parent or guardian. Have them read the Informed Consent Form and review the information, answering all questions. Once all questions have been answered, have the parent or guardian sign the form. Have the parent or guardian complete the Participant Demographics and Screening Record Form and verbally question the parent or guardian about the health history. Each parent or guardian will be asked if they want a copy of the consent form prior to release.
    a. Participants ranging in age 7–12 years will additionally go through an Assent process.
4. Based on the responses to the Participant Demographics and Screening Record Form and health assessment, record accepted or declined from the study. Continue if accepted into the study.
5. Position participant in the parent's lap, on bed, or in a chair (for pediatric participants).

6. Setup and verify communication between the devices and data collection systems.
7. Record device information for tracking (manufacturer, model #, serial/lot, hardware/software control info).
8. Record participant information, participant number, and demographics information.
9. Apply a SpO_2 sensor to the participant following the IFU for the pulse oximeter.
    a. Sensors may be placed on the feet or hands.
    b. Supplemental tape may be used to secure the sensors on feet that are too large for the sensor bandage length.
10. Apply the nasal cannula to the participant. Use neonatal/infant soft tape as necessary to adhere the nasal cannula.
11. Apply Device Under Test sensors to the participant per the IFU. Adjust sensors and devices as appropriate, ensuring the Device Under Test is producing valid outputs, and record the placement on test form.
12. Allow readings to stabilize for at least a few minutes.
13. Begin Respiratory Rate evaluation.
    a. Start data collection and elapsed timer display.
    b. Encourage the participant to be quiet.
    c. Mark in MediCollector quiet periods with minimal movement, talking, and/or crying. Note motion events, location, position, and activity level of the participant in the CRF.
    d. Data from the Reference ($EtCO_2$ waveform) and the DUT will be recorded continuously. Additional study notes that describe conditions of the test as well as deviations, device issues, and any adverse events will be recorded in written documentation.
    e. Record data for up to 60 minutes.
14. Remove all sensors and end the data collection.
15. The clinician will review any final questions with the parent or guardian and assess any effects from the study. The participant will be released with no further follow up required.

Statistical Analysis

Clinimark will perform the statistical analysis for the verification phase.

The Reference Respiratory Rate based on $EtCO_2$ will be collected simultaneous to the Device Under Test Respiratory Rate during one minute epochs during quiet, stable periods. The data will be paired based on syncing of the data collection system clocks. During the stable data sets, the DUT data will be averaged in approximately 60 second intervals. The Reference $EtCO_2$ waveform will be scored by counting the respiratory peaks per minute (See Appendix B: Sample Waveform Scoring Form for an example). The reviewers counting the raw $EtCO_2$ waveform will be blinded to the results from the test device.

The final pairing to be analyzed is Reference $EtCO_2$ scored and counted waveform with the average of the simultaneous 60 second period for the DUT. The Accuracy root-mean-square (A_{rms}) will be the basis for evaluation and acceptance.

Endpoint / Comparator

The primary objective of this study is to compare the accuracy of the device under test for the measurement of respiratory rate to the Reference, which is an End Tidal Carbon Dioxide Monitor ($EtCO_2$). For verification, the $EtCO_2$ waveform will be scored by counting the respiratory peaks per minute.

The endpoint of interest is accuracy as measured by the Accuracy root-mean-square (A_{rms}) difference between the Device Under Test (DUT) and the Reference Respiratory Rate as counted by $EtCO_2$ scored waveform (Ref) for all stable respiratory periods where

$$A_{rms} = \sqrt{\frac{\sum(DUT-Ref)^2}{n}}$$

Mean bias will also be generated:

$$Bias = \frac{1}{n}\sum_{i=1}^{n}(DUT_i - Ref_i)$$

Acceptance Criteria: Passing requires an A_{rms} of ≤3.0cpm.

Sample Size Justification

This study will utilize a sample size of 20 participants with 7 to 11 usable data points per participant, providing ≥200 data points over the specified breath per minute range.

Success for this study is defined as $A_{RMS} \leq$ 3cpm. The A_{RMS} statistic measures accuracy of a device under test (DUT) when compared to a reference device (REF) over a range of values. Accuracy, measured by the A_{RMS} statistic, can be affected by both random and systematic components of error. Here we estimate power to obtain an $A_{RMS} \leq$ 3cpm for this study through simulation using parameters estimated from two preliminary studies conducted previously by Clinimark. Respiratory rate study 1 composed of 894 data points from 18 study participants. respiratory rate study 2 composed of 913 data points from 20 study participants. Both studies had respiratory rate targets of 5, 10, 15, 20, 25, 30, 35, 40 and 45 breaths per minute. The A_{RMS} statistics are 2.8cpm and 1.2cpm for Study 1 and Study 2 respectively. For more information about the results and standard respiratory rate metrics please refer to 'Summary of Respiratory Rate Data and Results from Clinimark Studies' dated May 1, 2019. These preliminary data contain the features of real data, such as within participant correlation that is present due to repeated measurements on the same study participants. Note this sample size was conducted on studies with adult populations where paced breathing can be used to get a range of repository rates. Participants in this study will breathe at their natural rate.

Repeated measures within participants is a common practice in the pulse oximetry field but is known to potentially lead to within participant correlation, which is accounted for in these power estimates. Linear mixed models (LMM) were used to estimate parameters for each study in order to take into account repeated measures within participants. DUT was treated as the dependent variable. Participant was treated as a random effect, and REF was treated as a fixed effect. Parameter estimates from the mixed model were used as parameter estimates for simulations. The variance between participants in the mixed model results were used to model within individual correlation. Residual variance was used to model variance within participants. The estimated effect of REF was modeled as slope. The simulation model also incorporated mean bias. The simulation model was as follows:

$$DUT_{ij} = m \times REF_{ij} + B + \sigma^2{}_{between} + \sigma^2{}_{within}$$

- m = slope; B = mean bias; σ^2 = variance;
- i = measure; j = individual

Simulations were performed for the studies with a range of 10 to 38 individuals and 1 to 5 measurements at each respiratory rate target of 5, 10, 15, 20, 25, 30, 35, 40 and 45 breaths per minute, for a total of 145 different study size combinations. For each study size, 10,000 simulations were performed and the percentage of simulated studies that passed was taken as the estimate of power for that study size combination. Parameter estimates from study 1 resulted in the most conservative power estimates, and are as follows:

m:0.97039
B: -0.08434
$\sigma^2{}_{between}$: 0.4724
$\sigma^2{}_{within}$: 7.04

Based on parameter estimates from study 1 the following combinations study sizes would have >80% to obtain $A_{RMS} \leq$ 3cpm: (Participants x measurements) 27x9, 16x18, 11x27, 10x36. A study design with 30 participants and 18 measurements per participant has >80% power to obtain $A_{RMS} \leq$ 3cpm given the expectation that the device

performs the same as Study 1. Statistical modeling and simulations were performed using R (R 3.5.3 GUI El Capitan build, the R Foundation for Statistical Computing, 2016).

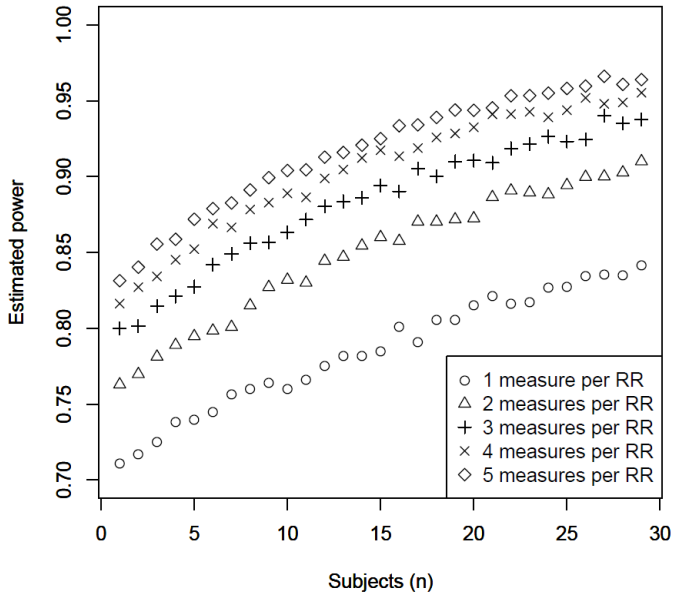


Figure 3 – Plot of estimated power based on the number of participants and measurements per respiratory rate

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

Prior to the start of participant enrollment, the primary 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 participant informed consent date. Written IRB/IEC approval and any conditions of approval imposed by the IRB/IEC will be obtained by the primary investigator.

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.

Monitoring Arrangements

Clinimark personnel (Louisville, CO, USA) 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:

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 Regulatory Authorities

Additionally:

- The conditions for the study continue to be acceptable

- Accurate, complete, and current records are maintained and required reports are written
- Any adverse effects are documented and reported to the Sponsor and IRB as appropriate
- Monitor activities may include for example: performing source data verification and requesting corrections to feedback forms where potential inconsistencies or missing values are identified.
- Findings of non-compliance or required modifications are reviewed with the investigator and the Sponsor, and is presented in a written report to both
- Providing a Monitoring Report at the end of the Clinical Investigation

Monitoring Plan

1) Informed Consent
   - Verify that the consent form was signed prior to any study procedures being conducted
   - Verify that the staff conducting the consent is listed for approval on the Delegation of Authority Log
   - Ensure that the consent process is documented.
2) Participant Eligibility
   - Verify that the participant meets the inclusion criteria and none of the exclusion criteria.
3) Baseline Data
   - Verify demographic information with the Participant Demographics and Screening Record Form
   - Check that informed consent time and date is prior to start of the procedure
4) Verify all CRFs are completed
5) Adverse Events
   - Verify that Adverse Events and Serious Adverse Events / UADEs are being reported accordingly to the IRB and Sponsor in the required timeframe.
6) Protocol Deviations
   - Verity that Protocol Deviations are being reported accordingly to the IRB and Sponsor in the required timeframe
7) Electronic Data Review
   - Verify that the filename matches the filename entered on the CRF
8) Ensure the Trial Master File is complete.

Data and Quality Management / Confidentiality

A checklist will be maintained identifying the contents of the Trial Master File / Project folder PFC# 2022-495.

The participant's name and parental signatures will be recorded on the Informed Consent, Participant Demographics and Screening Record Form, Assent Form (if applies), and a participant scheduling list. The data collection form will only use a participant number for the day of the test along with participant demographics. A name will not be recorded on the case report form.

Records identifying the participant's name will be kept in a secured location with either a locked file or locked door. Access to these files will be on a limited basis. Potential reviewers of this information include: Clinimark representatives collecting the information and conducting the study, Medical Director for Clinimark, Regulatory Authorities, Department of Health and Human Services (DHHS) agencies, Governmental agencies in other countries, Salus Independent Review Board and representatives of the Sponsor. This group may use the information to conduct independent audits and reviews to verify compliance of the regulatory requirements for these studies but not copy the information.

Data files stored electronically will be associated with a participant based off of participant #, date and by filename recorded on the data collection forms. The original device electronic data files will be preserved in its original form. Data analysis will be performed as a separate electronic file.

Data files, data collection records with participant demographics and participant number may be additionally copied, (after de-identification, if applicable) reviewed and supplied to the commercial sponsor for the study or Contractors associated with Clinimark for data analysis purposes.

All study records will be stored for at least 2 years post the release of the product or project cancellation. The investigator will notify sponsor prior to destruction of study records. Other storage arrangements may be executed per contractual agreement between the sponsor and the investigator.

Records - Study Documentation / Case Report Forms

Respiratory Rate Verification Study - Gabi SmartCare Gabi Band
Clinimark Study ID# PR 2022-495

Participant Documents

Provided as separate documents to this protocol:

- Parental Permission Informed Consent form (IRB approved)
- IRB Approved Assent Form - Assent Document For Minors 7 to 12 years of age
- 2022-495 Participant Demographics and Screening Record Form (F2000-001-009 modified for 2022-495)

Study Conduct Documents:

- CRF2022-495– Case Report Forms
- Electronic Files – electronic data collected from the reference and DUT systems

Data Collection Forms / Case Report Forms

To ensure the quality and integrity of the data, it is the responsibility of the Investigator(s) or designee to complete the Case Report Forms (CRFs) for each participant who is enrolled to participate in this study. In some cases, the data collection forms will also be the source document for some information that is not directly collected in the Health Assessment Form. The following information will be recorded on the site's data collection forms (CRF):

- Study date, Participant ID#, Participant Initials, and Relevant Participant Demographics, Associated Electronic Filename(s)
    - Participant demographics: gender, age, height, weight, race, ethnicity, skin tone
- Evidence that informed consent was signed and dated prior to the participant's involvement in the study
- Baseline vital signs pertinent to the inclusion and exclusion criteria (SpO_2, PR, Blood pressure, etc.)
- Information for Participant Inclusion or Exclusion to the study
- Equipment calibration and communication check out
- Device usage / sensor placement on the participant
- Annotations on data point markers, stability, and other observations used in the data analysis
- Protocol Deviation reporting (only if needed)
- Adverse Events reporting (only if needed)
- Device Deficiency reporting (only if needed)
- Study termination

A black or blue pen will be used to record data on the data collection forms. Recorded information should be legible and complete. Erroneous entries should be crossed out, corrected with the change, initialed and dated by the individual making the correction. The Investigator(s) or designee will sign and date at indicated places on each page of the data collection form. The Protocol Deviations Reporting can be signed and dated by the designee only if there are no deviations, otherwise the Sub-Investigator or Investigator should review, sign and date. The Adverse Events Reporting should be signed and dated by the designee and a Sub-Investigator or Investigator. The Principal Investigator needs to review, sign and date all serious adverse events. The Investigator or designee will provide a final signature indicating that a thorough inspection of all participant data has been performed and will thereby

certify the contents of the forms. The Investigator's Certification Statement will disclose the overall documentation, study oversight and certification of the study.

Trial Master File Documents

- Clinimark Control # B3000-000-003 - Adverse Events and Protocol Deviation Reporting System
- Clinimark Control # F2000-001-015 - Delegation of Authority
- Clinimark Control # F2000-001-016 - Device Accountability Form
- Clinimark Control # F2000-001-017 - Investigator Financial Interest Disclosure
- Clinimark Control # F2000-001-022 - Investigator's Certification Statement
- Clinimark Control # F2000-001-027 - Site Personnel Training Log
- Clinimark Control # F2000-001-028 - Subject Enrollment Log
- Clinimark Control # F2000-001-029 - Device Deficiency Form
- Clinimark Control # F2000-001-033 - Site Visit/ Monitoring Log
- Clinimark Control # F2000-001-034 - Data Clarification Form
- Clinimark Control # F2000-001-035 - Regulatory Binder Bullet Checklist
- Clinimark Control # F2000-001-037 - Protocol Deviation Log
- Clinimark Control # F2000-001-038 - Adverse Events Log
- Clinimark Control # F2000-001-042 - Adverse Event CRF
- Clinimark Control # F2000-001-043 - Protocol Deviation Form
- Clinimark Control # F2000-001-044 - Subject Screening Log
- Clinimark Control # F2000-001-052 - Device Deficiency Log
- Communications
- Additional documents include: Investigator brochure if provided, PI CV, key staff CV or resumes, Correspondence with IRB, IRB voting list, signed contract (optional), insurance certificates, shipping records, SIV / Monitoring documentation, names and contacts for key staff & sponsor, relevant sponsor correspondence, customer provided documentation, Final report.

Current revision of documents applies.

Amendments to the Clinical Investigation Plan

The sponsor or Clinimark may need to make protocol changes during the study. Such amendments will be documented, reviewed and changes will be submitted to the sponsor for first approval, then to the IRB for approval. The sponsor and site will make a decision regarding the continuation of participant enrollment during this period. The site may proceed with the amendment upon receipt of IRB approval.

Deviations from the Clinical Investigation Plan

Investigators are not allowed to deviate from the Clinical Investigation Plan (CIP) except under emergency circumstances. Deviations from the CIP to protect the rights, safety and well-being of human participants may proceed without prior approval of the sponsor and the IRB. Such deviations shall be documented and reported to the sponsor and the IRB as soon as possible but within 5 working days of the occurrence of such deviation.

Deviations that significantly affect the safety, efficacy, integrity, or conduct of the study must be reported to the Sponsor within 5 working days from awareness of occurrence and reported to the IRB per the deviation reporting policy.

Deviations that do not affect the safety, efficacy, integrity, or conduct of the study will be documented in the case report forms, regulatory binder Protocol Deviation Log as appropriate.

Device Accountability

A Device Accountability Log will be maintained for the sponsor's equipment documenting date of receipt, description of device (including model#, lot#, serial number or unique code, and quantity) and date of return for used and unused product. Device usage will be recorded in the Case Report Form for each individual participant.

Device Deficiencies

A Device Deficiency Log will be maintained during the study. Upon a device deficiency, a Device Deficiencies Form will be filled out and is also marked on the participant's CRF. Any device deficiency regarding the operation of the device or software or any malfunctions are to be reported to the sponsor. The sponsor will provide a follow up investigation to the deficiency.

Packaging and Labeling

Research conducted for this study will utilize investigational devices and devices cleared through the 510k regulatory process. The Sponsor is responsible for packaging and labelling of the device for delivery to the study site. Investigational devices or its immediate package shall bear a label with the following information: name and place of the manufacturer, packager, or distributor, the quantity of contents, if appropriate, and the following statement:

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

The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

It is the investigator's responsibility to ensure the appropriate labelling is visible and remains intact throughout the life of the study.

The Instructions for Use (IFUs) are provided as separate documents from this protocol.

Storage and Accountability

The site will store the investigational product. The storage area should be locked/secure with access limited only to approved study staff.

The site will record/track use of the investigational device by each participant. Documentation should verify that the device use was in accordance with the approved protocol. Equipment Document in the Case Report Form shall provide documentation of the devices used on the study participant(s).

Statement of Compliance

The study will be conducted in accordance with the Declaration of Helsinki, 21 CFR 50, and 21 CFR 812 for non-significant risk device study investigations. The study will not commence until the approval has been received from the IRB.

Reference Documents

IRB Approved Informed Consent for Study Title: Respiratory Rate Verification Study – Gabi SmartCare Gabi Band Study ID# PR 2022-495

- ISO 80601-2-61, first edition 2011-04-01, applicable sections, Clause 50 and Annex EE.3 Medical electrical equipment — Part 2-61: Particular requirements for basic safety and essential performance of pulse oximeter equipment
- FDA Guidance Document for Pulse Oximeters, March 4, 2013
- World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects
- ISO 14155:2011 Clinical investigation of medical devices for human subjects — Good clinical practice

  - FDA recognition of ISO 14155 Second edition 2011-02-01 will be superseded by recognition of ISO 14155 Third edition 2020-07. FDA will accept declarations of conformity to ISO 14155 Second edition 2011-02-01 until 18 December 2022.
- Clinimark Adverse Events Reporting Document B3000-000-003 (current revision)

Informed Consent Process

- The Principal Investigator or his / her designee conducts the informed consent process
- Verify that the participant's parents or guardian acknowledges ability to read English
- Instruct the participant's parent or guardian to ask questions at any time during this process, especially about things they do not understand.
- Allow participant's parent or guardian ample time to read the entire form and ask questions.
- Give a thorough description of the study and the participant's involvement – especially explain that the parent or guardian may withdraw the participant from study at any time.
- After the participant's parent or guardian has read the form ask if they understand everything
- Ask if they would like their child to take part in the study and if so explain that they may sign and date the form.
- Once the participant's parent or guardian has signed and dated the informed consent, the principal investigator or authorized designee will sign and date the form.
- Give a copy of the informed consent to the participant's parent or guardian
- No procedure may be performed before the informed consent is signed by the participant's parent or guardian

If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

Safety

Investigators

All experimenters must review the protocol prior to test and sign that they read and understood the contents.

Participant

Equipment is checked out for proper functionality prior to being placed on the participant.

The parents or legal guardians of the participant will review and sign the informed consent following a discussion of the test procedure and when all questions regarding the study have been answered and prior to start of any study procedures. The parents or legal guardians will complete the health assessment questionnaire and disclose any pertinent issues that may affect their child's health during the test. The parents or legal guardians of the subject may withdraw the participant from the study at any time. The participant may be withdrawn per the Procedure section below.

A clinician will be present to monitor the participant at all times. Safety monitoring includes, SpO_2, pulse rate, respiratory rate, direct observation and communication with the participant and parents or legal guardians.

Adverse Event Definitions

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

- **Adverse Device Effect (ADE):** Adverse event related to the use of an investigational medical device resulting from insufficiencies or inadequacies in the instructions for use, the deployment, installation, the operation, or any malfunction of the investigational medical device or from error use.

- **Adverse Event (AE):** Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in participants, users or other persons whether or not related to the investigational medical device or investigational procedure
- **Anticipated Serious Adverse Device Effects (ASADE):** ASADE is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.
- **Mild:** a mild adverse event is one in which the participant is aware of the event, but it is easily tolerated without intervention.
- **Moderate:** a moderate adverse event is one that causes sufficient discomfort to interfere with usual activities.
- **Serious Adverse Device Effect (SADE):** adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
- **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.
- **Severe:** a severe adverse event is one that results in the inability to perform usual activities.
- **Unanticipated Adverse Device Effect (UADE):** serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Management of Adverse Event Reporting

Should the participant experience an adverse or non-typical event, assessment of the situation is first initiated and a determination will be made of appropriate actions. The Medical Director and Principal Investigator will be contacted as appropriate. Adverse Events are reported through standard Clinimark Procedures, IRB requirements and per Gabi SmartCare SOPs.

Records of Adverse events will be recorded in the Case Report Form
The following information will be obtained:

- Type of effect (ADE, AE. ASADE, SADE, SAE, UADE)
- Date of onset and resolution
- Intensity (mild, moderate, severe)
- Serious (yes/no)
- Relationship to device (unknown, not related, possibly related, probably related, definitely related)
- Anticipated (yes/no)
- Treatment given and / or action taken (procedure stopped, withdrawn from study, no action)

Reporting of Serious Adverse Events and / or UADE

All SAE's, SADE, ASADE and UADE will be reported in writing to the Principal Investigator, Medical Director Sponsor and IRB as soon as possible and no later than 10 working days after the investigator first learns of the event.

If the event resulted in death of a participant, the event shall be reported to the Principal Investigator, Clinimark Medical Director, Sponsor and IRB within 24hrs of knowledge of the event.

Sponsor Records and Reports

Records 21 CFR 812.140 (b) 4,5

The following records shall be consolidated in one location and available for inspection and copying by Regulatory Authorities:

- The name and intended use of the device and the objectives of the investigation;
- A brief explanation of why the device is not a significant risk device:

- The name and address of each investigator:
- The name and address of each IRB that has reviewed the investigation:
- A statement of the extent to which the good manufacturing practice regulation in part 820 will be followed in manufacturing the device; and
- Any other information required by Regulatory Authorities
- Records concerning adverse device effects (whether anticipated or unanticipated) and complaints

Reporting 21 CFR 812.150 (b) 1,2,3,5,6,7,8,9,10:
The sponsor shall prepare and submit the following complete, accurate, and timely reports.

Unanticipated Adverse Device Effect
A sponsor shall immediately conduct an evaluation of an unanticipated adverse device effect. The results of such evaluation shall be reported to the Regulatory Authorities, IRB and participating investigators as soon as possible and not later than 10 working days after the investigator first learns of the effect.

Withdrawal of IRB approval
Withdrawal of IRB approval shall be reported to the Regulatory Authorities, IRB and the investigator within 5 working days after receipt of the withdrawal approval by the sponsor.

Withdrawal of Regulatory Authorities approval
Withdrawal of Regulatory Authorities approval of an investigation shall be reported by the sponsor to the IRB and the investigator within 5 working days after receipt of notice the withdrawal approval.

Progress Reports
The sponsor shall submit progress reports to the IRB at least yearly.

Recall and device
The sponsor shall notify Regulatory Authorities and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.

Final Report
The sponsor shall submit a final report to the IRB within 6 months after termination or completion of the investigation.

Informed consent
The sponsor shall submit to Regulatory Authorities a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.

Significant risk device determinations – (does not apply to NSR studies)
If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor shall submit to Regulatory Authorities a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.

Other
A sponsor shall, upon request by a reviewing IRB or Regulatory Authorities, provide accurate, complete, and current information about any aspect of the investigation.

Investigators Records and Reporting

Records 21 CFR 812.140 (a)(3)(i)

The investigator maintains records of each participant's case history and exposure to the device and supporting data including signed and dated consent forms, health assessment form, and progress notes during the study. Records should show evidence that informed consent was signed and dated prior to the participant's involvement in the study.

Reports 21 CFR 812.150 (a) 1,2,5,7

The investigator shall prepare and submit the following complete, accurate, and timely reports:

Unanticipated adverse device effects

The investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

Withdrawal of IRB approval

The investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

Informed consent

If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

Other

The investigator shall, upon request by a reviewing IRB or Regulatory Authorities, provide accurate, complete, and current information about any aspect of the investigation.

Withdrawal, Early Termination or Suspension of the Investigation

Participation in the study is voluntary. The parents or legal guardians may choose to withdraw the participant from the study at any point. If a participant officially withdraws from the study, the laboratory staff will document the reason for withdrawal in the case report.

Participation in the study may also be stopped at any time by the principal investigator or by the sub-investigators or sponsor.

- The participant's failure to cooperate fully (as determined by the investigator in his or her sole discretion) with the required conduct of this study.
- The participant's development of an illness as determined by the investigator in his or her sole discretion.
- A determination by a Clinimark representative (in his or her sole discretion), for whatever cause, that the study should be discontinued.
- A determination by the sponsor (in his or her sole discretion), for whatever cause, that the study should be discontinued

The collection of data for study participants will cease in the following cases:

- Participant completes all study requirements
- Participant's parent or guardian withdraw consent
- Investigator's decision that it is in participant's best interest to be discontinued from the study
- Participant death
- Adverse event other than death requiring withdrawal of the participant from the study
- Determination that the participant was ineligible for the study.

There will not be any follow-up procedures for withdrawn or discontinued participants required, unless a follow-up is required at the Investigator's discretion.

Consideration for early termination or suspension of the investigation is tied to unanticipated equipment failure or a decision by the sponsor or the site. Both Gabi SmartCare and Clinimark reserve the right to discontinue the study at any time for administrative or other reasons. Written notice of study termination will be submitted to the investigator in advance of such termination. Termination of a specific site can occur because of, but not limited to, inadequate data collection, low participant enrollment, or non-compliance with the protocol or other research requirements.

Early termination results when the study is closed prior to the end of the study. A study suspension is a temporary postponement of the study activities related to enrollment. Both are possible for the study. If the study is terminated or suspended, no additional enrollment will be allowed unless otherwise informed by the sponsor. The current participants will be followed according to the protocol.

If the study is terminated prematurely or suspended by the sponsor/investigator, the sponsor /investigator will promptly inform the regulatory authorities (if required) of the termination and the reason(s). IRB/IECs will also be promptly informed and provided with the reason(s) for termination or suspension by the sponsor/ investigator. The investigator will promptly inform the participants and assure appropriate follow-up for the participant.

If the investigator (or IRB/IEC) terminates or suspends the investigation the investigator will promptly inform the institution (if required) and the IRB/IEC, and provide a detailed written explanation of the termination or suspension. The investigator will promptly inform the participants and assure appropriate therapy and follow-up for the participants. The sponsor will inform the regulatory authorities (if required).

Withdrawal of IRB approval shall be reported to the sponsor by the investigator within 2 working days.

In case of early termination of the study, all study participants should be followed until the resolution of any pending adverse event(s).

Publication Policy

The results of this investigation may not be submitted for publication.

Attachment A - Protocol Signature Page

Protocol No. PR 2022-495

As the Principal Investigator, I confirm that I have read this protocol, I understand it, and I will work according to this protocol and to the ethical principles stated in accordance with the Declaration of Helsinki, 21 CFR 50, and 21 CFR 812: or the applicable laws and regulations of the country of the study site for which I am responsible, whichever provides the greater protection of the individual.

- Ensuring informed consent of each participant is obtained prior to the start of any study procedure
- Ensuring the investigation is conducted according to the Clinical Investigation Plan,
- Personally conducting or supervising the investigation,
- Protecting the rights, safety, and welfare of participants,
- Preparing and maintaining adequate, current, and complete case histories or records,
- Retaining records for two years following the date the marketing application is approved or withdrawn,
- Furnishing the required reports to the sponsor, including reports of adverse events and study completion,
- Providing timely reports to the IRB, including reports of changes in the research activity needed to avoid immediate hazards to participants, unanticipated problems involving risks to participants or others, including adverse events to the extent required by the IRB,
- Ensuring that changes are not implemented without prospective IRB approval, unless required to eliminate immediate hazard to participants,
- Complying with all FDA or Regulatory Authorities test article requirements,
- Adequately maintaining control of test articles, including appropriate tracking documentation for test articles to the extent that such control and documentation are not centrally administered,
- Supervising the use and disposition of the test article,
- Disclosing relevant financial information, and
- Ensuring that all associates, colleagues, and employees assisting in the conduct of the investigation(s) are informed about their obligations in meeting the above commitments.
- An investigator shall, upon request by a reviewing IRB, FDA, or other Regulatory Authorities provide accurate, complete, and current information about any aspect of the investigation.

_____	21 Sep 2022
Signature of Investigator	Date

Arthur Cabrera, MD
Investigator Name (print or type)

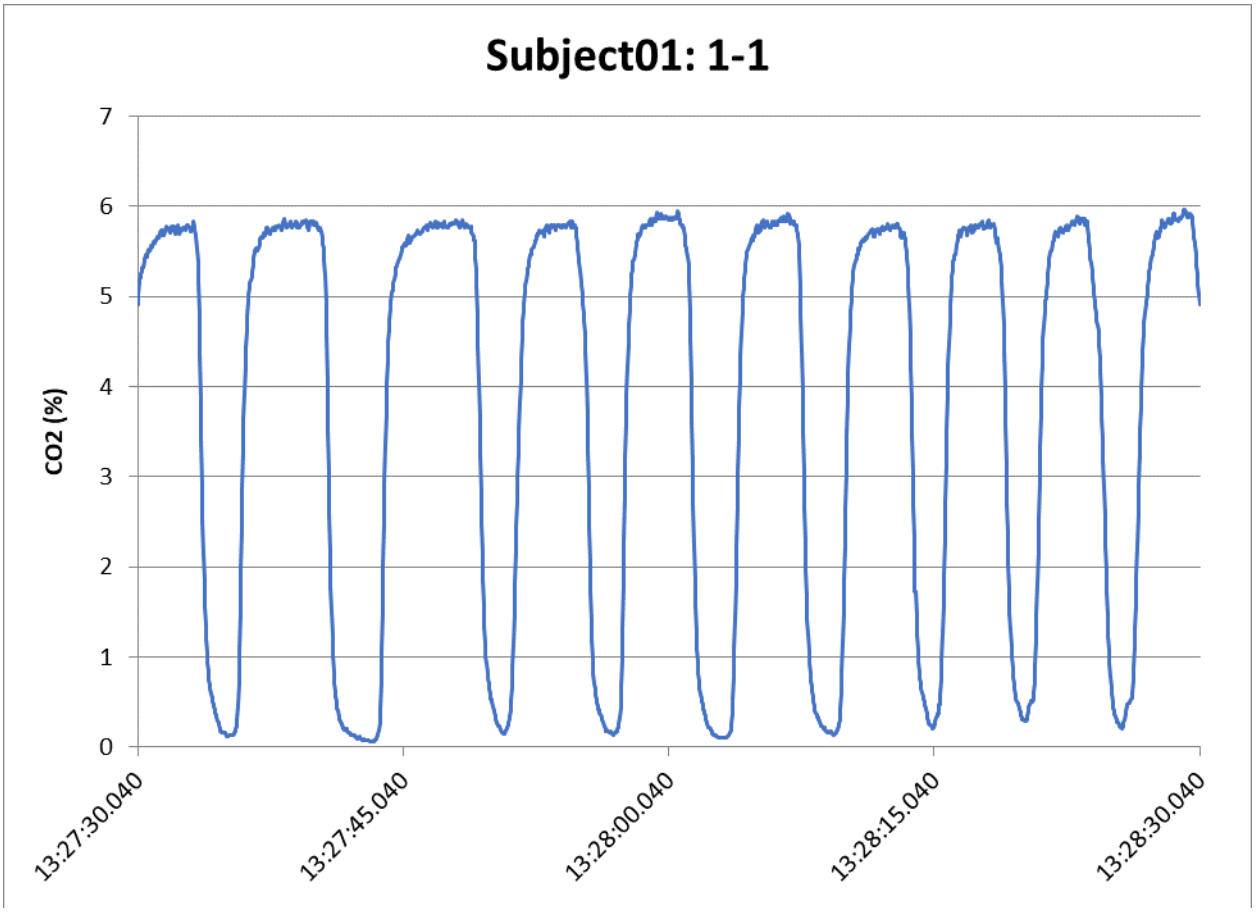
Principal Investigator
Investigator Title

Clinimark Laboratory
Name of Facility

Louisville, CO USA
Location of Facility (City, State, Country)

Appendix B: Sample Waveform Scoring Form

Below is an example of the waveform scoring form. The reviewers counting the raw $EtCO_2$ waveform will be blinded to the results from the test device.



Respiratory Rate _____

Scorer Name _____ Date _____

Checked by _____

Date _____