PIVOT BREATH SENSOR PERFORMANCE STUDY PROTOCOL [redacted] PROTOCOL NUMBER: [redacted]

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Synopsis

Device Names	1) Pivot Breath Sensor 2) Micro+™ Smokerlyzer®
Protocol Title	Pivot Breath Sensor Performance Study [redacted]
Principal Investigators	[redacted]
Co-Investigators	[redacted]
Protocol Number	[redacted]
Protocol Version	[redacted]
Sponsor	Carrot Inc., [redacted]
Study Design	Prospective, observational open label, single center study enrolling 70 subjects to evaluate performance of the Pivot Breath Sensor. No medical decisions will be made related to test results.
Primary Objective	Performance: • Non-invasively measure carbon monoxide (CO) levels in the exhaled breath of study subjects using two different types of measurement devices. • We will assess the correlation between the measured CO levels (in parts per million, or ppm) of the study CO breath sensor (Carrot Inc.) and the predicate CO breath sensor (Bedfont).
Potential Subjects	70 subjects who self-report smoking 2 or more cigarettes each day.
Inclusion Criteria	• 18-80 years of age • Owns and uses a smartphone • Willing to sign the Informed Consent Form • Resident of the United States • Able to read and comprehend English
Exclusion Criteria	• Prior experience with a study sponsored by Carrot Inc. • Pregnancy
Recruitment	Eligible subjects will be identified via a clinical research recruiter and/or advertisement at outdoor locations (i.e. flea markets, outside of movie theaters, shopping malls, train stations, stores that sell cigarettes), print media (i.e., local newspapers, billboards), and web media (i.e., Craigslist, Facebook).
Study Session	Single day study collecting 1 paired breath sample from each subject using two non-invasive breath sampling devices (Pivot Breath Sensor and Smokerlyzer), as well as collecting participant response to rating scales.
Performance Variable	CO concentrations in parts per million (ppm) in exhaled breath from subjects.
Performance Endpoint and Analysis	CO concentrations from each sensor type will be plotted for comparison.

Contents

1. LIST OF ABBREVIATIONS

CO	Carbon Monoxide
CRF	Case Report Form
USB	Universal Serial Bus
IRB	Institutional Review Board
ICF	Informed Consent Form
HCP	Health Care Provider
ppm	parts per million

2. INTRODUCTION

2.1 BACKGROUND

The smoking of tobacco products is a leading cause of preventable morbidity and mortality, excess health care expenditure, and lost work productivity. [redacted]

[redacted]

Since our 2018 study, Carrot Inc. (Redwood City, CA, USA) has made improvements to the CO breath sensor (the Pivot Breath Sensor). The Pivot Breath Sensor consists of a stand-alone handheld breath sensor to measure CO in exhaled breath with a display screen to show results. This breath sensor can optionally be used with a smartphone app (Pivot Application). The Pivot Breath Sensor is intended to be used as a personal and mobile product and to be available 'over the counter'.

This study will assess the performance of the Pivot Breath Sensor relative to the Micro+™ Smokerlyzer®.

2.2 STUDY RATIONALE

Performance: We aim to non-invasively measure carbon monoxide (CO) levels in the exhaled breath of study subjects using two different types of measurement devices. We will assess the correlation between the measured CO levels (in ppm) of the study CO breath sensor (Pivot Breath Sensor; Carrot Inc.; Redwood City, CA, USA) completed by a lay user with no personal instruction (using labeling only) and the predicate CO breath sensor (Micro+™ Smokerlyzer®; Bedfont Scientific Ltd; Harrietsham, UK) administered by a person trained to instruct users on submitting a sample with the device.

2.3 POTENTIAL RISKS AND BENEFITS

2.3.1 Known Potential Risks

There are no anticipated risks or harms to the subject. No medical decisions are made

based on study data.

2.3.2 Known Potential Benefits

While we do not anticipate that subjects will receive any benefit from their participation in this study, it is possible that some subjects may experience an increased awareness of their smoking behavior.

2.3.3 Risk Benefit Assessment

Given the non-invasive nature of the breath sampling and the data collection, there are no anticipated risks to subject safety. Study staff will be with subjects and monitoring their use of the study devices for the duration of the study. Subjects are not asked to change their smoking behavior. No medical decisions are made based on study data.

3. OBJECTIVES

We aim to non-invasively measure carbon monoxide (CO) levels in the exhaled breath of study subjects using two different types of measurement devices. We will assess the correlation between the measured CO levels (in ppm) of the study CO breath sensor (Pivot Breath Sensor, Carrot Inc.; Redwood City, CA, USA) and the predicate CO breath sensor (Micro^{+}™ Smokerlyzer®, ,Bedfont Scientific Ltd; Harrietsham, UK; 510K number: K082315).

4. REFERENCES

- FDA Guidance Document Entitled, "Guidance for Industry and Food and Drug Administration Staff: Applying Human Factors and Usability Engineering to Medical Devices," issued on February 3, 2016
- FDA Guidance Document Entitled, "Design Considerations for Devices Intended for Home Use, Guidance for Industry and Food and Drug Administration Staff" issued on November 24, 2014
- ISO/IEC 62366-1:2015, Medical devices – Application of usability engineering to medical devices. Geneva, International Electro technical Commission.
- AAMI/ANSI HE75:2009, Human Factors Engineering – Design of Medical Devices.
- https://www.bluetooth.com/what-is-bluetooth-technology/bluetooth-technology-basics

5. DEFINITIONS

Bluetooth Low Energy (BLE): a global wireless communication standard that connects devices together over a certain distance.

Objective Data: Data collected through direct observation.

Pivot Breath Sensor: The study device. It is a personal mobile breath sensor that is capable of measuring the level of carbon monoxide (CO) in exhaled breath. It is portable, battery-powered, and small enough to be carried by the user throughout the day (pocket, purse, backpack). The sensor is intended for single-user use by cigarette smokers to inform the user about how breath carbon monoxide levels are affected by smoking behavior. The user submits a breath sample by exhaling (blowing) directly into the mouthpiece connected to the sensor with breath sample results displayed on a screen on the sensor.

Subjective Data: Data collected through user feedback via responses to rating scales provided

by participants.

User: Person who interacts with (i.e., operates or handles) the Pivot Breath Sensor.

6. DEVICE DESCRIPTION

6.1 PIVOT BREATH SENSOR, STUDY DEVICE

The Pivot Breath Sensor comprises a personal mobile breath sensor that measures the level of CO in exhaled breath and displays the exhaled breath CO value to the user directly on the device. The range of CO measurement is 0-100 ppm.

The Pivot Breath Sensor (Figure 1) is portable, battery-powered, and small enough to be conveniently carried by the user throughout the day (pocket, purse, backpack). The Pivot Breath Sensor is rechargeable using a micro-USB cable. The user submits a breath sample by exhaling (blowing) into the mouthpiece of the Pivot Breath Sensor.

6.1.1 Indications for Use

The Pivot Breath Sensor is a breath carbon monoxide monitor intended for single-user use by cigarette smokers to inform the user about how breath carbon monoxide levels are affected by smoking behavior. The device is not intended to be used with other inhaled products.

Figure 1. Pivot Breath Sensor

6.2 LABELING AND PACKAGING

The Pivot Breath Sensor package includes:

- 1 Pivot Breath Sensor
- 1 USB charging cable
- 1 Replaceable Mouthpiece
- 1 Quick Start Guide [redacted]

The Pivot Breath Sensor packaging is shown in [redacted].

6.3 MICRO+™ SMOKERLYZER®, COMPARATOR DEVICE

The Micro+™ Smokerlyzer® (Bedfont Scientific Ltd; Harrietsham, UK; 510K number: K082315) is an FDA-cleared hand-held, battery powered instrument which uses

electrochemical technology to sample the gas and a microprocessor to convert the output from the sensor to a carbon monoxide (CO) concentration. The result and menus are displayed on a color LCD and an accompanying buzzer sounds in response to the CO level. The instrument is controlled using a touch screen operation. The range of CO measurement is 0-500 ppm.

Figure 2. Micro+™ Smokerlyzer® CO Breath Sensor

6.3.1 Indications for Use

The Micro+™ Smokerlyzer® is a Breath Carbon Monoxide Monitor intended for multi-patient use by healthcare professionals in smoking cessation programs and as an indicator of Carbon Monoxide poisoning in healthcare environments.

6.4 GASTROLYZER®, HYDROGEN MEASURING DEVICE®

Gastrolyzer® is a breath hydrogen monitor intended for multi-patient use by healthcare professionals in as an indicator of hydrogen produced gastrointestinal microbe based on diet of person and can indicate disorders such as lactose intolerance and carbohydrate breakdown deficiency. While the Gastrolyzer is not a comparator device, hydrogen may confound CO readings from CO breath sensors, so a measurement during the study is desired.

6.5 PIVOT BREATH SENSOR SUBMITTING A BREATH SAMPLE (SPECIFIC STEPS)

Submitting a breath sample involves the following steps. Instructions can be accessed in multiple locations including the Pivot Sensor's display screen, in the User Manual, Quick Start Guide, and on the packaging.

1. User presses any button to turn on the Pivot Breath Sensor.
2. User presses and holds the center button on the Pivot Breath Sensor until the sensor beeps once.
3. User takes a deep breath in and holds their breath for 10 seconds.
4. After about 10 seconds, the device beeps 3 times, and the user then will exhale slowly until the sensor vibrates at 12 seconds.
5. The user's CO level will display on the sensor's screen.

A properly submitted breath sample is defined as one that initiates after the third beep prompt and is of at least 6 seconds duration. Breath sensor hardware and firmware is capable of detecting when a breath sample submission starts and stops.

The CO Log screen in the Pivot Breath Sensor provides the CO (ppm) value for properly submitted breath samples, and provides a descriptive error message for improperly submitted breath samples (i.e. "Error: breath sample too late").

The computation of concentration of CO (ppm) is performed within the Pivot Breath Sensor firmware and the data (CO ppm concentration, time and date) are stored in the Pivot Breath Sensor memory.

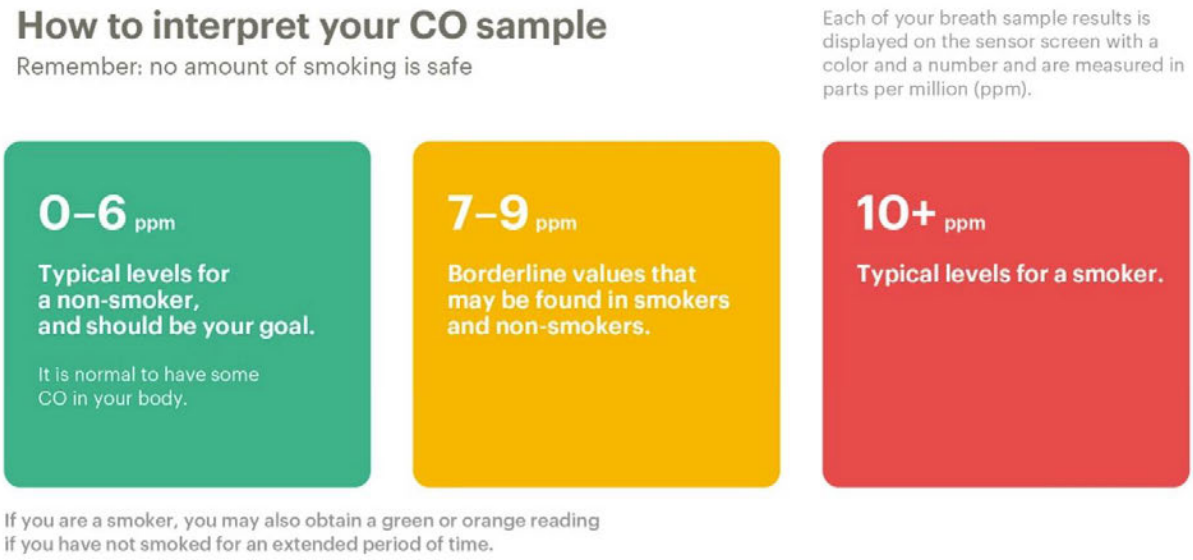
6.6 CO LOG

The CO Log can be accessed from the Pivot Breath Sensor's display screen and shows the most recent exhaled breath CO value in ppm at the top of the screen. The user can view previous values by scrolling within the log (Figure 3).

Values are color coded and can be interpreted by the user with help from the labeling (Figure 4).

Figure 3. CO log on Pivot Breath Sensor

Figure 4. Package labeling to interpret results



7. STUDY DESIGN AND OVERVIEW

7.1 STUDY DESIGN

This is a prospective open-label performance study conducted with IRB approval enrolling 70 subjects who report daily smoking at our research center [redacted] or an equivalent location. Subjects will be asked to set up the Pivot Breath Sensor and provide a breath sample using the device during a 60-minute session. No follow-up visit is required.

7.2 STUDY ENDPOINTS

Comparison of paired breath sample values from the study and predicate devices.

7.3 ELIGIBILITY CRITERIA

The intended user population for the Pivot Breath Sensor System are lay users who are smokers, ages 18-80, capable of using a smartphone to track/monitor health-related data. The intended users range in age, degree of smoking, mental and physical capabilities, health literacy, experience using other CO analyzers or home use medical devices, and experience using smartphones.

Study participants will consist of individuals who represent the intended user profile, current smokers. Participant criteria include all of the following:

Inclusion Criteria

- 18-80 years of age
- Current daily cigarette smokers (at least 2 cigarettes per day with target distribution of individuals who smoke: 2-5 cigarettes per day, 6-10 cigarettes per day, 11-15 cigarettes per day and 16+ cigarettes per day)
- Resident of the United States
- Able to read and comprehend English

- Currently own and use an Apple, Inc. iPhone iOS smartphone or an Android smartphone for at least one month (such that they are familiar with basic operations of the mobile platform)
- Willing to sign the Informed Consent Form

Exclusion Criteria

- Prior experience with a study sponsored by Carrot Inc.
- Pregnancy

7.4 SUBJECT RECRUITMENT

Subjects will be recruited in the United State by a clinical research recruiter and/or through advertisement at outdoor locations (i.e. flea markets, outside of movie theaters, shopping malls, train stations, stores that sell cigarettes), print media (i.e., local newspapers, billboards), and web media (e.g. Craigslist, Facebook, Task Rabbit, Google Ads) [redacted]. Respondents will be asked to provide contact information (phone number, email address), and answer questions on demographics (gender, age), smartphone ownership and smoking behavior using the Online Screening Form [redacted] or through the clinical research recruiter, if applicable. Study staff will review each potential participant's responses to the eligibility questions.

Potential subjects may also convey their interest in participating in the study by calling or emailing study personnel using the contact information provided in the recruitment materials, or responding to outreach from the clinical recruiter.

All study participants will undergo a screening call where they will be asked questions to confirm study eligibility. During this call, study personnel will inform the potential subject of the study details and will answer any questions. Eligible participants who meet the inclusion/exclusion criteria will be offered the opportunity to participate in the study. Potential subjects will then determine if they would like to proceed with scheduling, and if so, study personnel will schedule the subject for a test session. At the test session, an Informed Consent Form [redacted] will be signed prior to participation.

7.5 SUBJECT STIPEND

Participants will be compensated $100 in the form of a Visa Gift card for the test session lasting approximately 60 minutes. Participants will be compensated at the end of their study session.

7.6 SAMPLE SIZE AND JUSTIFICATION

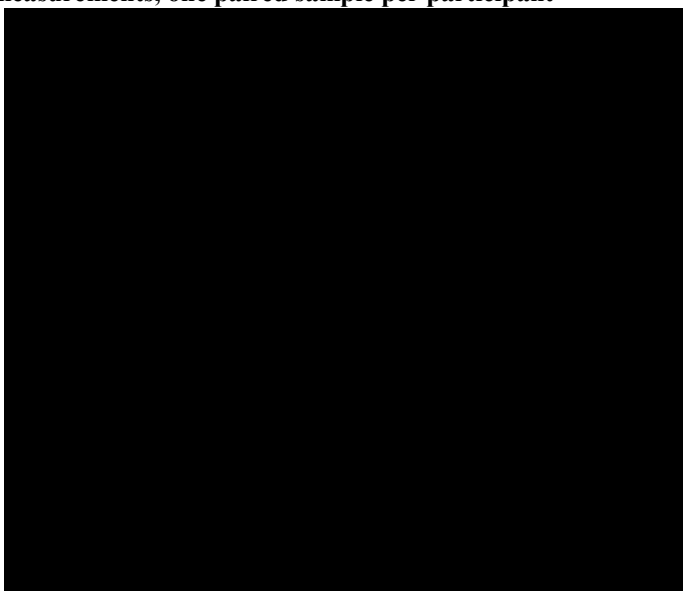
This study will include 70 subjects. This sample size is expected to provide adequate data to compare CO measurements between the devices. Sample size needed was determined as described below.

Data from formative studies was used to develop the statistical methodology for the present study. We conducted formative studies titled [redacted], with approval by the Institutional Review Board. The studies were conducted with signed informed consent. [redacted]

[redacted]

Figure 5a. Study [redacted] Correlation of Pivot Breath Sensor and Smokerlyzer CO (ppm) breath sample measurements, three paired samples per participant.

Figure 5b. Study [redacted] Correlation of Pivot Breath Sensor and Smokerlyzer CO (ppm) breath sample measurements, one paired sample per participant



We performed power calculations based on the null hypothesis that the Pearson correlation coefficient of the predicate and Pivot Breath Sensor was [redacted] and the alternative hypothesis that it was greater than [redacted]. Assuming a true Pearson correlation of [redacted], if we collect [redacted] samples from predicate and study devices, we will have [redacted] power to reach statistical significance assuming a 0.05 alpha level (red circle on graph, Figure 6). Further, assuming a true Pearson correlation of [redacted], if we collect [redacted] samples from predicate and study devices, we will have [redacted] power to reach statistical significance assuming a [redacted] alpha level (orange circle on graph, Figure 6). Based on this formative data analysis, our validation study will include 70 subjects (70 subjects who report daily smoking).

Figure 6. Sample Size power calculation scenarios

[redacted]

7.7 STUDY ARTICLES

Pivot Breath Sensor in representative packaging [redacted] that includes:

- Pivot Breath Sensor
- USB charging Cable
- Replaceable Mouthpiece
- Quick Start Guide [redacted]

In addition, the testing room will be equipped with electrical outlets and a charging cube.

7.8 EQUIPMENT AND MATERIALS

- A pre-set Pivot Breath Sensor with example CO breath samples, or a CO Log Print Out
- Printed prompt cards for the participant to reference
- Timer or clock
- Video recording equipment
- Camera
- Post-it notes
- Quick Start Guide for study staff
- User Manual for study staff
- Electronic Surveys
- Case Report Forms

A full list of equipment and materials used during the study will be recorded in the report.

7.9 USER MANUAL AND TRAINING

The Pivot Breath Sensor was designed to be as intuitive as possible, such that users are able to understand how to use the product on their own. No in-person training is formally offered to Pivot Breath Sensor users. A Quick Start Guide and package labeling is included with the device to aid the user and an online User Manual [redacted] is also available. All of these items will be accessible to the study participant plus a phone and a phone number within the labeling material to contact technical support. Since in-person training will not be formally offered to all users who purchase the Pivot Breath Sensor, in-person training will not be included in this study. Study participants will have access to the aforementioned materials.

While participants will have the User Manual, Quick Start Guide and packaging available to them at any point during the study, they will not be asked to read instructions or use any of the forms of training available.

7.10 TEST ENVIRONMENT

The study will be performed in an office building conference room or office.

7.10.1 Location testing will be performed:

The location of testing will [redacted] For example, office space may be rented to be nearer to test subjects.

7.11 STUDY PERSONNEL

The study team members will be trained by reading the study protocol and reviewing the case report forms. The study team members will have full training on the operation of the study devices.

7.12 IRB OVERSIGHT

This study will be conducted under IRB oversight.

8. STUDY PROCEDURE

Each study session will have the following format:

1. Introduction and informed consent
2. Device Setup
3. Breath Sampling and Interpretation
4. Rating Scales

At the beginning of the 60-minute test session, subjects will have ample time to read the Informed Consent Form (ICF) and the opportunity to ask questions. The subject will sign the ICF before participating in this study. Once signing the ICF, the subject will be given a unique identifier to protect subject privacy. Subjects may choose to exit the study at any time. They are not required to complete the study if they choose to stop.

Study participants will self-train on how to use the study device using only the available study Pivot Breath Sensor device labeling, including product packaging, Quick Start Guide, a technical support line (phone number provided in packaging/Quick Start Guide), and User Manual. These labeling materials will be available to study participants at any point during the study. Study participants will not be asked to read instructions or use any of the forms of training available. Study personnel will refrain from answering questions on how to use the study device during the study.

After completing baseline questions (age, gender, ethnicity, pregnancy status, smoking history and behavior, use of smoking cessation medications, issues with vision/hearing, smartphone type, attitudes towards smoking, past use of carbon monoxide breath sensors) participants will be provided the Pivot Breath Sensor package. They will be instructed to start using the product. Upon initiating use of the product, participants are automatically taken through a self-training that is delivered through the labeling and device. Study staff will observe but not deliver any components of this training. Completing self-training includes the successful completion of at least one breath sample. Participants will be asked how that went for them, and allowed to repeat a breath sample until they indicate they are satisfied with their breath sample Once the study participant has completed the self-training on the Pivot Breath Sensor, they will be asked to interpret their own breath sample results as well as hypothetical breath sample results. They will be asked if they feel ready to proceed with submitting a breath sample. If a participant indicates they do not feel ready, they will be asked to do what they would normally do at home to prepare to use the product and to let the test administrator know when they are ready to submit a breath sample.

When the participant indicates readiness to provide a breath sample, he/she will be instructed to proceed to provide one breath sample using the study device. This is the performance breath sample. Participants will be asked how that went for them, and allowed to repeat a

breath sample until they indicate they are satisfied with their breath sample. After providing this breath sample, the subject will be asked to interpret his/her breath sample result. This will be followed by a breath sample using the predicate device. A test administrator will instruct the participant how to give this breath sample before proceeding, and will direct the participant through the breath sample in real-time. This will be followed by a breath sample using a breath sensor that measures hydrogen in exhaled breath (Gastrolyzer®, Bedfont Scientific Ltd; Harrietsham, UK). This measurement is obtained because hydrogen levels can impact carbon monoxide readings on the Micro^{+}™ Smokerlyzer® device. A test administrator will instruct the participant how to give this breath sample before proceeding, and will direct the participant through the breath sample in real-time.

Next, participants may be asked to refer to the Pivot Breath Sensor labeling to answer questions regarding interpretation of other possible breath sample results (optional). This is followed by obtaining participant input using rating scales.

As needed, photo and video recordings may be implemented during the study to facilitate post-study analysis.

9. DATA COLLECTION

Study personnel will collect information about the participant including

- Age
- Gender
- Pregnant?
- Race/ethnicity
- Vision
    - Wear glasses?
    - Color blind?
- Hearing
    - Hearing issues?
    - Use a hearing aid?
- Type of smartphone participant uses (iPhone or Android)
- Number of years smoking
- Number of quit attempts over the past 12 months
- Number of cigarettes currently smoked per day
- Smoking history in the past 24 hours
    - Number of cigarettes smoked
    - Time of last cigarette
    - Use of any combustible, inhaled tobacco product other than cigarettes (pipes, cigars, cigarillos, etc.), any electronic cigarette product (e-cigs, vape, vapor), and any other inhaled combustible material
- Attitudes towards smoking
    - Desire to quit
    - Readiness to quit

  - Confidence to quit
  - Perceived difficulty of staying quit
- Current smoking cessation medications
- Participation in a smoking cessation program
  - Past
  - Present
- Breath sensor use (past)
  - Use of CO breath sensors in the past
- Breath sensor use during the study session
  - Model#/Serial# of breath sensor
  - CO measurements

10. TECHNICAL APPROACH AND STUDY DESIGN

10.1 ACCEPTANCE CRITERIA

Data will be accepted if the participant meets eligibility criteria and completes breath sampling, including providing a sample from the predicate device, as instructed.

11. STUDY RESULTS

11.1 DATA COLLECTION AND CONFIDENTIALITY

Subjects will be assigned a unique subject ID which will be used for data collection. Data collection will take place on paper or electronic case report forms (CRFs) completed by the study team and study subjects. CRFs will be reviewed by the study team prior to the end of the study session to ensure completeness and then stored in a secure filing cabinet at the end of the day with access limited to necessary study personnel. Study data will be kept in a secure database by the investigator. This database will be accessible only by necessary study personnel. The database will not contain personal identifying information; all subject data in the database will be associated with study identification numbers. The data will be kept for a minimum of 5 years.

11.2 ANALYSIS

11.2.1 Performance

A paired breath sample is defined as subject submitting a breath sample unassisted using the study device, and submitting a breath sample assisted by a health care professional (or test administrator) using the predicate device.

- Participant breath sample CO measurement done with the study device compared to the CO measurement of the participant's breath sample done with the predicate device.
- Participant's interpretation of results will be tallied for correct interpretation

11.2.2 Subjective data

Subjective data will include:

- Participant ratings which will be summarized.

11.3 REPORT

A final report will be issued upon completion of testing, allowable in PowerPoint format, and will include the following:

- Report must include testing details such as description of products tested and identification numbers.
- Report must identify staff members who tested and evaluated/inspected samples. Test date(s) must be identified.
- Report must identify any deviation from the protocol, and any anomalies in sample testing. Justification and approval of deviation must be documented.
- Report must include test results section and must identify any changes to the testing samples.
- Report must include summary of rating scales data
- Report must be signed by the primary investigator or study team designee. It must also be reviewed and approved by the study team.

11.4 DEVIATIONS FROM PROTOCOL

To be determined by the study team during performance study. Deviations will be assessed through a consensus review of the study team. All deviations will be identified, recorded and analyzed in the final report.

11.5 RECORD RETENTION

Record keeping is performed in accordance with the SOP Control of Quality Records, [redacted]

12. CONFLICTS OF INTEREST

The following conflicts of interest are noted:

- The study sponsor is Carrot Inc., [redacted]
- The principal investigator and co-investigators own equity in Carrot Inc., which is the company that invented and owns the Pivot Breath Sensor, which is being evaluated in this study.
- The company (Carrot Inc.) holds patent rights to one of the devices being evaluated in the study (the Pivot Breath Sensor).

The investigator (Jennifer Marler, MD) holds a position of senior management officer, as Sr. Director of Clinical and Medical Affairs. The Co-Investigator (Craig Fujii, BS), holds a position of Director of Clinical Affairs. The Co-Investigator (Kristine Wong, BS), holds a position of Senior Clinical Research Associate. These conflicts of interest are mitigated by the following:

- The risk profile of the study, specifically, that there are no anticipated risks or harms to the subject. No medical decisions are made based on study data. The process of setting up the Pivot Breath Sensor and providing breath samples is non-invasive, and

done under the observation and support of trained study personnel. Study participants will be able to indicate how they are feeling and if they would like to continue or discontinue giving breath samples.

- The role of Carrot Inc. in the study is outlined in the study Informed Consent Form; participants will be aware of this role prior to providing informed consent.
- The aim of the study is to assess the performance of the Pivot Breath Sensor in intended users and then use this data to optimize the product as needed. This study will inform resultant improvements made to the Carrot Inc. products (the Pivot Breath Sensor). As such, it is imperative, and the goal, that the study sponsor uses this data to ensure its products are as user-friendly and accurate as possible.

13. [redacted]

[redacted]

14. LITERATURE REFERENCES

[redacted]

15. DOCUMENT REVISION HISTORY:

Rev. A	Original Protocol

Rev. B Updated and provided more explicit detail for study session flow in Section 8: baseline questions-self-training-subjective input-interpret results-performance breath sample-subjective input-predicate breath sample-hydrogen breath sensor breath sample-interpret results using labeling materials-rating scales.