Tool Revision History:

Version Number	Version Date	Summary of Revisions Made
0.1	20 Feb 2018	Original version

Introductory Clinical Trial for Measuring Patients Before, During, and After an Electrophysiology (EP) Procedure with a Novel, Body-Worn Sensor

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Additional Investigators:	N/A
NYULMC Study Number:	*S17-01618*
ClinicalTrials.gov	NCT03657134
Funding Sponsor:	N/A
IND/IDE Number:	CoVa™ 2 is a Class 2 medical device (K160899) that received 510(k) approval from the FDA in June 2017 for measurments of HR, HRV, RR, TEMP, FLUIDS, SV, and CO.
Regulatory Sponsor:	N/A
Study Product:	CoVa Monitoring System 2
Study Product Provider:	toSense, Inc.

Initial version: A

List of Abbreviations

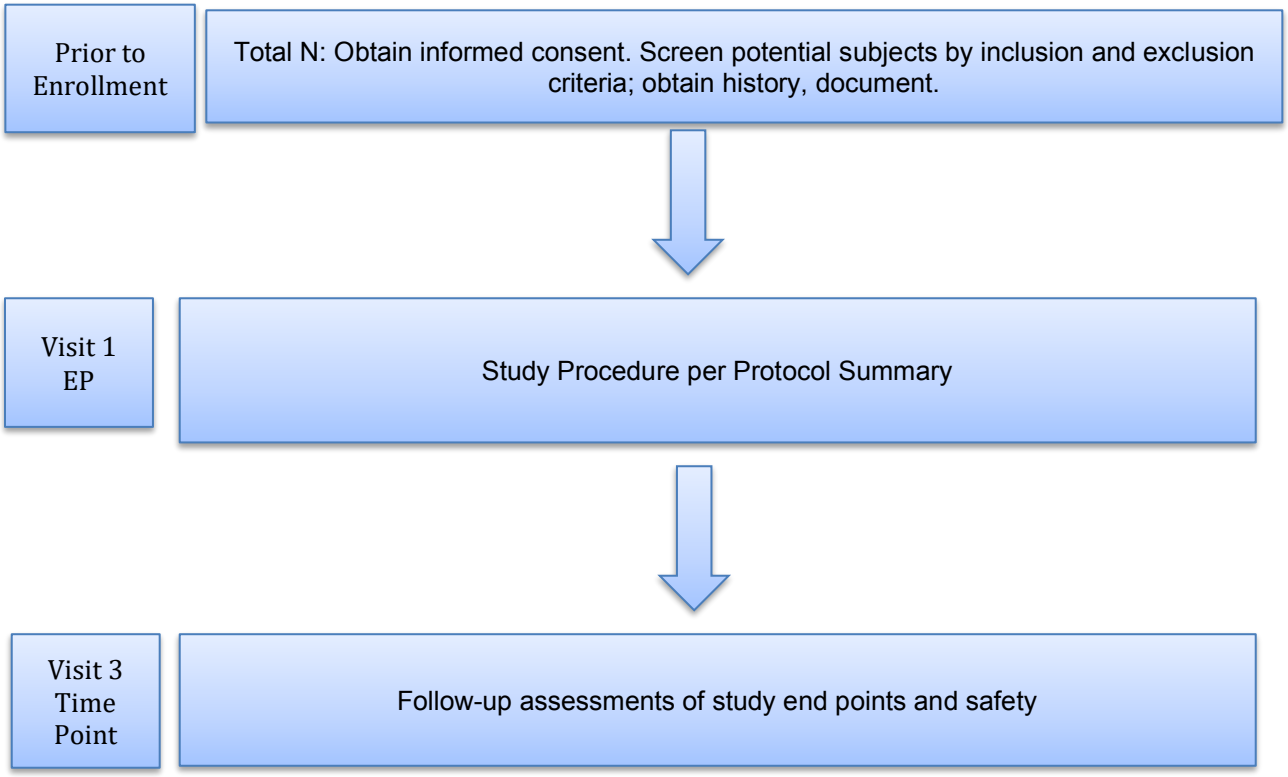
AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CO	Cardiac Output
CoVa™ 2	CoVa™ Monitoring System 2
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
ECG	Electrocardiogram Waveform
EP	Electrophysiology
FLUIDS	Thoracic Fluids Measured with Impedance
GCP	Good Clinical Practice
HR	Heart Rate
HRV	Heart Rate Variability
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ISM	Independent Safety Monitor
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
RR	Respiration Rate
SOP	Standard Operating Procedure
SV	Stroke Volume
TBI	Thoracic Bioimpedance Waveform

Protocol Summary

Title	Introductory Clinical Trial for Measuring Patients Before, During, and After an EP Procedure with a Novel, Body-Worn Sensor
Short Title	NA
Brief Summary	Subjects will be consented to wear the CoVa™ 2 prior to, during, and after after an Electrophysiology Procedure. During this time, the system will measure the following parameters from subjects: HR, HRV, RR, TEMP, FLUIDS, SC, and CO. Data will be retrospectively analyzed to determine if the system effectively operates under these conditions, and can effectively monitor subjects and allow them to be discharged early from the hospital. Subjects will not be measured while transferred in and out of the operating room. Approximate sample size is 20 subjects.
Phase	N/A
Objectives	The primary objective of this study is to show that, when used before, during, and after an EP procedure, CoVa™ 2 is able to successfully measure vital signs, waveforms, and hemodynamic parameters from patients, indicate the efficacy of the EP procedure, and show any signs of patient decompensation or complications. An additional objective of this study is to show that, through use of CoVa™ 2, patients can be discharged relatively early from the hospital after undergoing an EP procedure.
Methodology	No randomization or blinding methods will be used for this study.
Endpoint	The primary endpoint will be if at least 50% of subjects studied in this trial are able to be discharged relatively early from the hospital if they are monitored with CoVa™ 2. A detailed retrospective statistical report will be the determining factor in meeting this success criteria.
Study Duration	Approximately 6 months
Participant Duration	Up to 7 days (until hospital discharge).
Duration of IP administration	N/A
Population	Approximate sample size: 20 subjects. Subjects are those which need an EP procedure,, including atrial fibrillation and SVT, pacemaker or ICD implant.
Study Sites	NYU Medical Center Electrophysiology 550 First Ave, Level 5 New York, NY 10016
Number of participants	20 subjects across one site

Description of Study Agent/Procedure	Subjects will be measured with CoVa™ 2 before and after an EP procedure.
Reference Therapy	N/A
Key Procedures	EP
Statistical Analysis	Statistical comparison (e.g. correlations) of measurements made before, during, and after the EP procedure to prove or disprove the above-mentioned study hypothesis.

Schematic of Study Design



1 Key Roles

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Introduction, Background Information and Scientific Rationale

Current hospital monitoring typically involves manually measuring conventional vital signs—such as blood pressure, heart rate, respiration rate, temperature, and pulse oximetry—initially every 15 minutes and than every few hours. This entire suite of vital signs is necessary, as it is rare that a single parameter can predict patient decompensation; more often, especially with complex disease states, all the vital signs (and often even more parameters) are required. And while not overly complicated, this process can be time consuming and inefficient. A clinician (typically a nurse, although increasingly someone with less training) enters the patient's room, straps to the patient a blood pressure cuff (around the brachium), an oximeter (on the finger), a thermometer (in the ear), and sometimes ECG leads (affixed to the chest), takes a series of

measurements, and then removes these sensors. The entire process takes about 5-10 minutes. Often measurement values are simply written down and transcribed later. Moreover, measurement of more sophisticated parameters, or measurements made outside of the hospital, are rarely done. In the hospital setting, parameters like stroke volume and cardiac output are typically only made with highly invasive or complicated devices requiring specialty-trained technicians, such as a pulmonary-arterial catheter or Doppler ultrasound machine. Patients are almost never discharged early and measured in the home, as the devices and infrastructure to enact such protocols do not exist.
The sensor used in this clinical trial, is a low-cost, easy-to-use, body-worn system that cures the deficiencies listed above. It will ultimately measure all vital signs, along with stroke volume, cardiac output, and fluids, non-invasively and from a single location on the patient's body. This sensor can be coupled to a cloud-based system for data analytics that generates timely, actionable information for clinical staff regardless of patient setting (e.g. in either the home or hospital). With such a system, patients could be discharged early or monitored at home to prevent readmissions. This may improve patient outcomes, since delays in recognition of a change in status often lead toward longer hospital stays and, in some cases, patient morbidity and mortality.

Name and Description of the Investigational Agent

toSense's CoVa™ 2 features a body-worn Sensor, Gateway, and Web-based System. The Sensor perform measurements by non-invasively sensing and processing single-lead ECG and TBI waveforms. Algorithms on the device processes these two waveforms to measure HR, HRV, RR, TEMP, FLUIDS, SV, and CO.

The Sensor has a form factor similar to a conventional necklace, with the electronics built into its strands and base. To make a measurement, a pair of customized disposable Electrodes—each featuring two electrode regions—snaps into a magnetic interface on the backside of the base and then attaches to the patient's chest. The Sensor is typically used for measurement periods less than 5 minutes but can also be used for longer periods (e.g. several hours or days).

Using a Bluetooth™ transceiver, the Sensor wirelessly transmits measurement information from the patient to a Gateway, such as a tablet computer or mobile phone running the Android operating system. These systems receive information from the Sensor, and then forward it to the Web-based System through either a local-area network (e.g., network based on 802.11), or a wide-area cellular network (e.g. AT&T). The Web-based System displays information and can forward it to a third-party system through a web-services interface.

CoVa™ is FDA-cleared (K160899) for the measurements described above.

Clinical Data to Date

See attached documents.

Known Potential Risks

Electrodes placed on the body may cause a slight redness or irritation. In rare cases, there is an allergic reaction or sensitivity to the adhesive that is used to stick the electrode patch. However, the adhesive that is used is not unique to this study, and is used in many medical applications. Discomfort could also occur when the adhesive patches are removed.

Known Potential Benefits

Subjects involved in this study will receive additional monitoring and may be discharged from hospital earlier as a result.

Objectives and Purpose

Primary Objective

When used before, during, and after an EP procedure, CoVa™ 2 is able to successfully measure vital signs, waveforms, and hemodynamic parameters from patients, indicate the efficacy of the EP procedure, and show any signs of patient decompensation or complications. Related to this primary objective is the goal of answering the following questions: Can data generated by CoVa™ 2 allow patients to be discharged from the hospital relatively early and monitored at home?

Secondary Objectives (if applicable)

In addition to the primary study objective, investigate the following questions: 1) can measurements made by the CoVa™ 2 (particularly stroke volume (SV), cardiac output (CO), fluid status, arrhythmia detection, and basic vital signs) be successfully made before, during, and after an EP procedure?; 2) is there correlation between CoVa™ 2-measured parameters (particularly volume status, heart rate and arrhythmia, SV, and CO) before, during, and after an EP procedure?; 3) does RF ablation during an EP procedure interfere with CoVa™ 2 measurements?; 4) does a 200-300 Joule shock during a DC cardioversion procedure interfere with CoVa™ 2 measurements?; and 5) is the CoVa™ 2's usability suitable for hospital clinicians?

Description of Study Design

Study subjects scheduled for an EP procedure who have signed an informed consent form (ICF) will be admitted to the study. Prior to the EP procedure (e.g. in a hospital room or operating room at NYU Medical Center), an employee of NYU will prep the subject's skin with an alcohol wipe, apply the CoVa™ 2 Sensor using a pair of disposable electrodes, connect it to the Gateway Device using Bluetooth®, and ensure that it is transmitting information from the CoVa™ 2 Sensor through the Gateway Device to the Cloud-based System. All transmitted information will be de-identified. All subjects will continue to be monitored with standard of care equipment.

Once this data pathway is verified, measurements will be made from the subject for a period of approximately 2 hours prior to the EP procedure. More specifically, measurements will be made continuously for a period of about 90 seconds, and then, as described above, information will be transferred from the CoVa™ 2 to the Gateway Device, and from the Gateway Device to the Cloud-based System. This process will take roughly 120 seconds. Once it is complete, this 'duty cycle' will be repeated for the duration of the 2-hour period, i.e. measurements will again commence for a period of about 90 seconds, and then paused for about 120 seconds while data is wirelessly transmitted as described above.

Measurements will be temporarily halted as the subject is moved into the operating room and prepped for the EP procedure. Prior to the procedure, the CoVa™ 2 sensor will be attached to an external power supply as described above. Once the procedure is started, measurements will be made in the same manner as described above.

Once the EP procedure is complete, the subject will be transferred from the operating room to a hospital room, where they will stay overnight. Measurements will be made during this period, but not while the subject is being transferred. Once the subject is situated in the hospital room, the CoVa™ 2 Sensor will be applied to the subject and connected to the external power supply in the same manner as described above. Then measurements will commence according to the same duty cycle as described above.

The patient will continuously wear the CoVa™ 2 system until they are discharged for a period of about 24 hours. During this period, data from the sensor will be sent to the Gateway and Cloud-based System, and then analyzed retrospectively.

During the course of the study, scientists at toSense will use the Data Analytics Software to process measurement information from CoVa™ 2, with a focus of proving or disproving the study's primary hypothesis, i.e. when the CoVa™ 2 Sensor is used before, during, and after an EP procedure, can it successfully measure patients, indicate the efficacy of the EP procedure, show any signs of patient decompensation or complications, and allow a patient to be discharged relatively early?

More detailed analyses will investigate the study's secondary objectives, i.e.:1) can measurements made by the CoVa™ 2 Sensor be successfully made before, during, and after an EP procedure; 2) is there correlation between parameters such as volume status, heart rate and arrhythmia, SV, and CO before, during, and after an EP procedure; 3) does RF ablation during an EP procedure interfere with CoVa™ 2 Sensor measurements?; 4) does a shock during a DC cardioversion interfere with CoVa™ 2 Sensor measurements?; and 5) is the usability of the CoVa™ 2 Sensor adequate before, during, and after an EP procedure suitable for clinicians?

Upon completion of the study, a report will be drafted describing the above-described information. The report may evolve into a peer-reviewed publication if this is determined by the PI to be an appropriate course of action.

This measurement protocol will be performed for a period of at approximately 6 months.

Study Endpoints

Primary Study Endpoints

The primary endpoint will be if at least 50% of subjects studied in this trial are able to be discharged relatively early from the hospital if they are monitored with CoVa™ 2, as determined through a retrospective analysis. A detailed retrospective statistical report will be the determining factor in meeting this success criteria.

Study Enrollment and Withdrawal

Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Patients with arrhythmias and other cardiac conditions that are scheduled for EP procedures.
2. Subject is over 22 years of age at the time of consenting
3. Subject and/or legally authorized representative is willing to undergo the informed consent process prior to enrollment in the study

Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Pregnant subjects
2. Subjects who are participating in another clinical study that may affect the results of either study

3. Subjects who are unwilling or unable to wear the sensor (and electrodes) for a period of up to 14 hours
4. Subjects who are considered by the principle investigator to be medically unsuitable for study participation

Vulnerable Subjects

Vulnerable subjects will not be utilized in this study. In the case of a vulnerable population patient being identified; they will not be included in the study or analysis..

Strategies for Recruitment and Retention

No NYULMC media will be used to recruit subjects. Subjects that are scheduled for an EP procedure and meet the inclusion criteria will be approached for enrollment.

Subjects will be consented in a quiet and private environment. Subjects will be given the opportunity to take the written consent form home to review overnight.

Use of DataCore/Epic Information for Recruitment Purposes

This study will utilize EPIC to identify subjects. Once potential subjects have been identified, the study team will notify the treating physician (TP) that they have patients eligible to participate. The study team will obtain approval from the treating physician to approach the eligible patient for the study.

Duration of Study Participation

The total duration of study participation is about 1.5 days. This includes:

Written Informed Consent Process: 1 day

Study Procedure: 1 day

Measurement prior to EP Procedure: 1-3 hours

Measurement after EP procedure: Patient will be measured until they are discharged from hospital (approximately 24 hours).

Subjects may be contacted for a follow-up interview.

Total Number of Participants and Sites

This is a single-site study. Recruitment will end when approximately 20 participants are enrolled. It is expected that approximately 20-30 participants will be recruited in order to produce 20 evaluable participants.

Reasons for Withdrawal or Termination

Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study if:

- Any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

Handling of Participant Withdrawals or Termination

Withdraw criteria:

- The Principle Investigator will review whether a withdrawal of a subject affects the success criteria of the study. A subject may be replaced if it is determined that more subjects are needed based on this criterion

Premature Termination or Suspension of Study

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or terminationIf the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the IRB.

Study Agent (Study drug, device, biologic, vaccine etc.) and/or Procedural Intervention

Study Agent(s) and Control Description

Acquisition

toSense will ship CoVa™ 2 systems directly to the Electrophysiology supplies team at the NYU medical center.

New York Medical Center
31st street and East River Drive,
TCH 576, EP Lab
New York, NY
10016

Devices will only be shipped once. The sensors should be kept as instructed in the product and stability section of this protocol.

Formulation, Appearance, Packaging, and Labeling

Devices are labeled with the follow symbols:

	Keep Dry
	Type BF – applied part
	Non-defibrillation proof device
	FCC certified
	Read Usage Instructions
	Single Use Only
	Necklace is MR Unsafe. Necklace should not be worn during MR Scan
	Wireless Transmission

Each device is labeled with a unique identifier (UID). The proposed product is available to human use in its current form.

Product Storage and Stability

Environmental Conditions for the CoVa™ Monitoring System 2		
Condition	**Storage (Packaged / Unpackaged)**	**Operating (Unpackaged)**
Temperature	-25°C to +70°C -13°F to +158°F	-5°C to +50°C 22°F to +122°F
Humidity	up to 93% non-condensing	10% to 93% non-condensing
Atmospheric Pressure Range	700 hPa to 1060 hPa	700 hPa to 1060 hPa
Shelf Life	Necklace: 6 months Electrodes: 2 years	Necklace: 6 months Electrodes: 24 hours

Device Specific Considerations

Physical Characteristics:

- Dimensions: 1cm H x 18.0 cm W x 30 cm L (0.4 in H x 6.5 in W x 13 in L)
- Weight: 0.127 kg (4.5 oz)
- Battery Type: Li-ion

Administration of Intervention

Devices will be placed on consented subjects either directly by the PI or qualified research staff.

Procedures for Training Interventionalists and Monitoring Intervention Fidelity

toSense will provide CoVa™ 2 on-site training to the PI, study staff and Co-Investigators.

Study Procedures and Schedule

Study Specific Procedures

CoVa™ 2 systems will be set up and attached to patients according to procedures described in toSense's FDA-cleared documentation.

Screening

The study team will screen for eligible patients using EPIC. Approval to approach eligible patients will be obtained from the TP. No research related activites will be conducted until eligible patient's have signed the consent form.

Enrollment/Baseline

The PI will confirm prior to enrollment that each subject qualifies for the study. The eligible subject will be approached by the research team. All patients willing to participate will personally sign and date the latest IRB approved version of the consent form. Written and verbal versions of the participant information and informed consent will be presented to the participants detailing no less than: the exact nature of the study; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal. The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their general practitioner or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. A copy of the signed Informed Consent will be given to the participants. The original signed form will be retained at the study site, in a research binder maintained by the study team in a locked cabinet. All documents will be stored safely in confidential conditions. On all physical and electronic study-specific documents, other than the signed consent, the participant will be referred to by a study participant number/code, not by name.

Visit 2 (Day of EP procedure)

- Ensure the subject has no additional questions regarding the study
- Once the subject has been prepped for surgery, apply the sensor to the subject's upper chest using the toSense approved electrodes
- Connect the device to the power source
- Study participant will be assigned a study number/code

- All data transmitted by the CoVa2 device will be de-identified.
- Run several test measurements on the sensor to ensure that the device is actively measuring on the subject
- Explain to the subject that the sensor will measure for a 90 seconds period, with 120 second pause in between measurements
- Measurements will not be made while the subject is transferred to and from the surgery room
- Measurements will be made until the patient is discharged
- Immediately prior to discharge, a study team member will remove the CoVa™ 2 device from the patient, and ensure a final data transmission.
  Withdrawal/Early Termination Visit

If the subject withdraws from the study:

- A reasonable attempt should be made to find out why the subject dropped out of the study
- Subjects may be replaced in the study
- Record the whether to withdrawal was from either the subject or principle investigator

Ethics/Protection of Human Subjects

Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

Informed Consent Process

Consent/Assent and Other Informational Documents Provided to Participants

Consent forms describing in detail the study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study product. The following consent materials are submitted with this protocol:

- Informed Consent Form

Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their

comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

A copy of the signed informed consent document will be stored in the subject's research record. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject's research record. Any alteration to the standard consent process (e.g. use of a translator, consent from a legally authorized representative, consent document presented orally, etc.) and the justification for such alteration will likewise be documented.

The consent process will take place at NYU medical center. Subjects will be consented in a private office prior to discussing any parts of the study. Subjects will be given an opportunity to read the consent form prior to signing. Those who are trained to consent will ensure the subject understands that this study is completely voluntary and will not affect the relationship with the PI or medical center. The informed consent form will be written in such a way that the subjects understands the language and procedures involved in the study.

Subjects who do not speak English are not specifically targeted in this study.

Participant and Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Participant confidentiality is strictly held in trust by the participating investigators an study staff. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party

Study members, and representatives of the IRBmay inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at NYU Langone Medical Center. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by NYU Langone Medical Center research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the NYU Langone Medical Center.

Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of data.

The data file will include password protection

Study Records Retention

Study documents will be retained for 5 years after final reporting/publication

Costs to the Participant

There are no costs to participants in this study

Participant Reimbursements or Payments

Subjects will not be compensated for participating in this study.