# Clinical Protocol

**Engineering Evaluation of the Vector NIV Device in Chronic Obstructive Pulmonary Disease (COPD) Patients**

Protocol # SRC-HRC-Vector ENG -2018-10241

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**Sponsored by**

**Respironics, Inc., a Philips Healthcare Company**
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**Protocol Title:** Engineering Evaluation of the Vector Device in Chronic Obstructive Pulmonary Disease patients

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**Reporting of Adverse Events or Adverse Device Effects**

Report the occurrence of an adverse event or adverse device effect to Philips Respironics within 24 hours of the occurrence.

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# Protocol Approvals

**Investigator Agreement.**
As Investigator of the study entitled "Engineering Evaluation of the Vector NIV Device in Chronic Obstructive Pulmonary Disease (COPD) Patients." Protocol # SRC-HRC-Vector ENG -2018-10241, I agree to:

(i) conduct the Study in accordance with: this Investigator Agreement; the Study's Protocol as approved by the IRB (the "Protocol"); all applicable laws and regulations; Good Clinical Practice and the Declaration of Helsinki; and any IRB or FDA conditions of approval;

(ii) await IRB approval for the Protocol before obtaining informed consents;

(iii) ensure that all requirements for informed consent are met and not let any subject participate in the Study before obtaining that subject's informed consent;

(iv) not make modifications to the Protocol as supplied to me by Respironics, Inc. (the "Sponsor"), without first obtaining the written approval of the Sponsor;

(v) provide the Sponsor with accurate financial information as required by FDA regulations;

(vi) supervise all testing of investigational devices that involves any Study subject;

(vii) maintain Study documentation for the period of time as required by FDA regulations;

(viii) will supply to the Sponsor, as part of this Investigator Agreement, my curriculum vitae.

**Investigator Signature**: _____ **Date**:_____

**Printed Name**: _____

# Protocol Revisions

| Revision Level | Changes Made to Protocol | Date | By |
|---|---|---|---|
| 1.0 | Initial Submission | 10/SEP/2018 | C. Cain, M. McDermott, B. Romano, D. White, J. McKenzie, K. Davis, B. Miller |
| 2.0 | Response to IRB comments | 20/SEP/2018 | B. Miller |
| 3.0 | Repeat Screening Visit and correction to overnight titration protocol | 17/Dec/2018 | B. Miller |
| 4.0 | Addition of 2 week at home use sub-study | 04/APR/2019 | C. Cain, B. Miller, K Davis |
| 5.0 | Update to participant compensation for take home portion | 29/APR/2019 | K. Davis, B, Miller |
| 6.0 | Update to repeat 2 week take home | 15/JUL/2019 | K. Davis, B, Miller |
| 7.0 | Addition of new research site and market research firm | 06/SEP/2019 | B. Fink (previously Miller) |
| 8.0 | Change of PI and clinical site | 29/SEP2019 | B. Fink |

# Glossary

**Apnea:** the cessation of airflow at the nostrils and mouth for at least 10 seconds.

**Apnea/Hypopnea Index (AHI):** the number of apneas and hypopneas per hour of sleep.

**Auto Adjusting Continuous Positive Airway Pressure Device:** A type of CPAP machine that monitors changes in breathing and compensates automatically by making appropriate therapeutic adjustments in pressure delivery.

**Average Volume Assured Pressure Support (AVAPS):** Positive airway pressure support that provides a gradual pressure change based on the average of the preceding several breaths.

**Bi-Level PAP Therapy:** Responds to both inspiration and expiration by the patient and delivers a set amount of pressure when the patient begins spontaneous inhalation and decreasing pressure when exhalation begins.

**COPD:** Chronic Obstructive Pulmonary Disease

**CPAP Pressure:** pressure needed to maintain an open airway in a sleep apnea patient treated with CPAP, expressed in centimeters of water (cm H20). The positive pressure can range from 4 - 25 cm H20. Different patients require different pressures. The value is determined in a CPAP titration study.

**CPAP Therapy:** Continuous Positive Airway Pressure – delivers a constant pressure during inspiration and expiration.

**Hypersomnolence:** Excessive daytime sleepiness.

**ODI:** 4% Oxygen Desaturation Index

**EFL:** Expiratory Flow Limitation **-** occurs when the airways become compressed which usually results when a pressure outside the airway exceeds the pressure inside the airway

**EPAP:** Expiratory Positive Airway Pressure**-**Physician prescribed pressure for the expiratory (breathing out) phase of an individual on Bi-level PAP therapy

**$FEV_1$:** Forced Expiratory Volume in one second – the volume of air exhaled in the first second of the FVC maneuver and is the most reproducible measurement of airway obstruction.

**FOT:** Forced Oscillation Technique – A method to detect the presence of expiratory flow limitation.

**FVC:** Forced Vital Capacity – Spirometry measurement in which the patient inhales maximally and then exhales as rapidly and completely as possible.

**IPAP:** Inspiratory Positive Airway Pressure **-** Physician prescribed pressure for the inspiratory (breathing in) phase of an individual on Bi-level PAP therapy.

**Noninvasive Positive Pressure Ventilation (NPPV):** mechanical ventilation provided noninvasively (by mask or similar interface) rather than through an endotracheal tube or tracheostomy.

**Positive End Expiratory Pressure (PEEP)**: Pressure in the lungs (alveolar pressure) above atmospheric pressure (the pressure outside of the body) that exists at the end of expiration.

**OSA:** Obstructive Sleep Apnea **-** a disorder in which complete or partial obstruction of the airway during sleep causes loud snoring, oxyhemoglobin desaturations and frequent arousals.

**S Mode:** Spontaneous Ventilation – provides ventilation in synchrony with a person's spontaneous breathing efforts; triggering of a breath cycle is only by the patient.

**S/T Mode:** Spontaneous Timed Ventilation – provides ventilation in synchrony with a person's spontaneous breathing efforts; triggering of a breath cycle is by the patient or the ventilator, should the person fail to trigger the ventilator after a preset time. In Spontaneous/Timed mode a "backup" rate is set to ensure that the patient still receives a minimum number of breaths per minute if they fail to breathe spontaneously.

**$Z_{rs}$** – total impedance of the respiratory system as measured by the forced oscillation technique (FOT) at a forcing frequency of 5 Hz.

**$X_{rs}$** – the reactance (i.e. the imaginary component of the impedance) of the respiratory system as measured by the forced oscillation technique (FOT) at a forcing frequency of 5 Hz.

**$\Delta X_{rs}$** – is the difference between the mean value of $X_{rs}$ during expiration ($\overline{X}_{exp}$) and the mean value of $X_{rs}$ during inspiration ($\overline{X}_{insp}$). A breath is classified as flow-limited if its $\Delta X_{rs}$ is greater than 2.8 $cmH_2O \cdot s \cdot L^{-1}$

# Background Information

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide.

Treatment options for COPD patients consist of medications, such as bronchodilators and anti-inflammatory drugs, pulmonary rehabilitation, long term oxygen therapy (LTOT), lung volume reduction surgery and lung transplantation. Studies have shown that bronchodilators and anti-inflammatory drugs show minor or no benefit on long term outcomes but rather are used mainly for symptomatic relief.[1] Pulmonary rehabilitation has been demonstrated to improve functional status and symptoms but there is lacking evidence on long term outcomes of this therapy. [2] Lung volume reduction surgery and lung transplantation is only appropriate for a small number of patients; therefore, there is no demonstration of improved long-term survival rate.[3, 4]

Of these available therapies, few have been shown to significantly improve long term patient outcomes. For the severe COPD patient, LTOT is the only treatment that demonstrated prolonged survival in controlled studies. [5, 6] But, despite the effectiveness of LTOT, COPD is still characterized by a high morbidity and mortality rate.

Noninvasive positive pressure ventilation (NPPV) is one therapy that may prove beneficial to stable COPD patients. NPPV is the use of positive pressure ventilation administered via a nasal or full face mask (that covers both the nose and mouth). This type of ventilation has become a well-established and increasingly used therapeutic option for patients with hypercapnic respiratory failure (HRF) due to COPD.[7]

NPPV, used nocturnally, may improve nighttime hypoventilation that is common with COPD patients. An improvement in nocturnal hypoventilation would reset the respiratory center sensitivity for $CO_2$.[8 9] This would result in an improvement in daytime gas exchange and sleep quality. It is also known that hyperinflation in patients with COPD increases their work of breathing, thus fatiguing the respiratory muscles.[10] It has been suggested that by applying nocturnal NPPV it would allow the respiratory muscles to rest, resulting in muscle function recovery, increased respiratory muscle strength, reduced the tendency for fatigue and improvement in pulmonary function and gas exchange.[11]

COPD is a disease that results in varying degrees of dyspnea, or shortness of breath. Spirometry is a method of diagnosing COPD with the presence of a post bronchodilator FEV1 <80% of the predicted value in combination with an FEV1 / FVC <70%. This would confirm that there is a presence of airflow limitation that is not fully reversible.

The presence of airflow limitation has been identified as one of the main causes of dyspnea in patients with chronic obstructive pulmonary disease (**1**). Expiratory Flow Limitation (EFL) occurs when the airways become compressed which usually results

when the pressure outside the airway exceeds the pressure inside the airway. As airflow obstruction worsens, EFL appears at much lower flows for a given lung volume and it becomes present at rest or at least develops early during exercise (**2**).

Early detection of EFL consisted of either invasive esophageal balloon or relatively complex plethysmographic techniques. An alternative approach, and one that will be used in this study, involves the Forced Oscillation Technique (FOT).

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## Description of the Intervention Studied

The Vector ventilator is intended to provide non-invasive ventilatory support to treat adult patients with Respiratory Insufficiency with the primary cause being COPD. It is intended to be used within the home, institutional/hospital, and diagnostic laboratory environments. This device is not intended for life support. It can be used to screen for the presence, and abolishment of Expiratory Flow Limitation.

The Vector ventilation method auto-titrates PEEP or EPAP on a breath by breath basis. Vector is a new noninvasive method to continuously detect EFL during spontaneous breathing and minimizing it using EPAP.

The device has been designed to produce a 5 Hz sine wave with peak to peak amplitude of approximately 2 cmH2O superimposed upon the pressure and flow generated by the device. The resultant feedback waveform is then filtered and analyzed to detect the change of a reactance (ΔXrs). Subsequently the EPAP (and concurrently and proportionally the IPAP) is increased until the EFL is essentially abolished (falls below the predetermined EFL threshold). Since this reactance is analyzed continuously (breath by breath) during both inspiration and expiration, it is relatively immune to external factors such as modest leaks or coughing/swallowing. Given that forced oscillation technique can be easily applied during noninvasive nasal ventilatory support, it could be used during routine noninvasive ventilation.

This Vector screening mode is an automated five-minute screening test can be done in a clinical environment under supervision to determine if EFL is present.

The screening test will have built in logic that determines the test's validity during the screening, as well as, the conclusion of the test. The screening test will be at a relatively fixed pressure (typically between 3-4 cmH2O) that will remain constant throughout the session. The screening session results, which will consist of near real-time pulmonary mechanic information will be kept on a display until the next session is enabled.

# Study Design Rationale

The clinical study is designed primarily as an engineering evaluation to verify the software functionality and performance of both the screening and therapy modes of the Vector device. This study is necessary in order to confirm the device is functioning as designed prior to use in larger clinical trials to support product launch.

# Study Objectives and Purpose

**Primary Objective**

The primary objective of the study is to collect engineering pre-therapy screening and therapy data on the Vector NIV device via an overnight study on COPD patients that have been identified as having EFL.

**Study Hypothesis:**

1. Therapy provided by the Vector device will minimize COPD patients' EFL throughout the course of an overnight sleep study

2. Clinical study staff can operate the Vector device to successfully screen patients for EFL and then set up the Vector device to determine the Optimized EPAP required for abolishment of EFL

**Study Endpoints:**

- Ventilator-collected parameters during the therapy night such as: Mean EPAP, Respiratory Rate, Minute Ventilation, and ΔXrs values.
- Ventilator-collected parameters during the EFL screening; ΔXrs value, % flow limited breaths, mask leak values.
- $SpO_2$.
- Patient Therapy comfort assessment via Questionnaires

# Study Design:

This study is a nonrandomized, unblinded overnight engineering clinical evaluation of the Vector NIV device in COPD patients with EFL. Up to 50 individuals may be enrolled in order to have a total of up to 30 completed participants. Male and female participants who qualify per the inclusion/exclusion criteria may be enrolled.

Potential participants will be identified and recruited from the site database of COPD patients. Potential participants may also be identified by a local marketing company. These participants will complete online or phone screenings prior to being seen at the clinical site.

**Schedule of Events:**

Participants will be contacted by designated study staff from the site database of COPD patients. Participants may be pre-screened over the phone to determine eligibility. Participants that are interested will be scheduled for the screening visit at the clinical office.

Potential participants may be also be found by a local marketing company. This marketing company will utilize their local database to find potential participants in the Pittsburgh, PA area. These participants will undergo a brief online and/or over the phone screening by the marketing company. If they are found to be potentially eligible, Philips Respironics study staff will reach out to the participants. A more thorough phone screen will be conducted by the Philips Respironics study staff. If the person is still found to be potentially eligible for the study and is interested they will either be scheduled by the Philips Respironics staff to come into the Pittsburgh Pulmonary Physician Practice site or will be contacted by the staff of Consolidated Clinical Trials for appointment scheduling. A waiver of informed consent for screening will be submitted to the IRB for contacting these participants.

Study Visit 1 (screening)

Once the participant arrives, the study will be explained in full detail. If the participant agrees, he/she will be consented into the study and the participant will be given a copy of the informed consent.

Once consent is obtained and eligibility is confirmed, the following study related procedures will be conducted:

- Demographics: gender, age, ethnicity, height and weight will be collected.
- Current Medications: all current medications will be collected.
- Medical History Assessment: information will be collected regarding historical spirometry data, COPD history and other relevant medical history including the diagnosis of sleep disordered breathing.
- Physical examination with vital signs to include HR, BP, RR, $SpO_2$ maintained at least 88%, and chest auscultation.
- Administration of CAT and EFL Indication questionnaires
- Mask Fitting: Participants will have a mask fitting in order to determine the best possible provided mask while using the Vector NIV device during the screening for EFL.

EFL Screening/Determination and EPAP Titration

- For the EFL Screening/Determination and EPAP Titration procedure, the study device will be set up in fixed pressure mode (Appendix A) for EFL.

- EFL Determination: The participant will be asked to breathe quietly into the Vector device using the selected mask for 5 minutes in the seated position, and then an additional 5 minutes while in supine or semi-recumbent position. This device has the capability of detecting EFL. If it is determined that the participant does not have EFL after 5 minutes by the device screening indicator, the participant will not continue in the study.

- EPAP Titration: if it is determined by the Vector NIV device that the participant has EFL, the Vector NIV device will be changed from screening mode to therapy mode to delivery BiPAP therapy. The participant may be changed to a new mask at this time. The participants will then breathe on the Vector NIV device in the supine position for approximately an additional 20 minutes. During the additional 20 minutes of breathing, the device will automatically increase the EPAP (and concurrently and proportionally the IPAP) until the EFL is abolished (or falls below the predetermined EFL threshold).

- While the automatic EPAP Titration is being performed, all participants' $SpO_2$ will be monitored via finger pulse oximetry. If the $SpO_2$ persistently falls below 88% during the titration, the participant will not be scheduled for study visit 2.

- Patient must stay awake during the EPAP Titration. If the patient, falls asleep, they will be woken by study staff.

- The Final EPAP that is determined to abolish the participants EFL will be recorded. If the determined EPAP pressure is 6cmH2O or higher, the participant may continue to study visit 2. If the determined EPAP is below 6cmH2O, then the participant will not be scheduled for study visit 2.

- EFL Screening Post Visit 1 Questionnaire

Participants that are determined to have EFL and a titrated EPAP >6cm H2O will be scheduled for study visit 2 where they will undergo an overnight sleep study with the Vector NIV device in a Sleep Laboratory.

<u>Study Visit 2 (Overnight Sleep Study) (within 28 days of visit 1 +/- 7 days)</u>

Participants will be asked to report to the sleep lab for an overnight sleep study. Participants will be asked to come to the sleep lab at a scheduled date and time in order to have the trained sleep technician along with a Philips Respironics engineer prepare them for the sleep study and re-acclimate them to the NIV device. The sleep testing will begin near the subject's usual bedtime and ends at you normal wake-up time.

For the sleep study, participants will be set-up with a standard PSG montage that will include the following sensors:

- Two RIP belts secured around the chest and abdomen to measure movements associated with breathing effort
- A small sensor which attaches to the chest belt to measure body position
- Lead II ECG electrode derivation
- EEG electrodes attached to the scalp and face to measure sleep stages (including at least C4, C3, A1, A2, O1, O2, GND EEG, Left Outer Canthus (LOC) and Right Outer Canthus (ROC) EOG and submental EMG)
- A flexible finger sensor placed on the finger to measure oxygen saturation (average signaling time of 3 seconds)
- A microphone attached to the skin at the base of the neck to measure snoring sounds
- Surface electrodes attached to the skin bilaterally over the anterior tibialis muscle, to measure leg movements

Prior to the sleep study with the NIV device, the trained technologists will verify mask size, fit, and adjustment that was determined at study visit 1. Patients will be asked to bring their previously fitted mask from the study visit 1. Once the sleep testing has started, technologists will have a 2 hour window from sleep onset to make any additional mask changes or adjustments.

During the Sleep study, the Vector NIV device will be connected to a laptop computer where all Ventilator related parameters collected by the device can be viewed and monitored by the sleep technician and the Philips Respironics engineer. These outputs include the device IPAP and EPAP pressures, EFL value, patient flow, mask leak, minute ventilation, and respiratory rate. A flexible finger sensor will be placed on the finger in order to measure and monitor oxygen saturation

During the sleep study, the Vector NIV device with the optimized EPAP will be tested in periods with both fixed pressure support as well Average Volume Assured Pressure Support during the night. In the event that the study participant presents with any obstructive or respiratory related events during the sleep study during the Vector therapy, the trained sleep technician will be able to make manual adjustments to the device pressure settings in order to address the issue (Appendix A).

In the event that manual titration was unsuccessful, the trained sleep technologist will refer to standard of care procedures including, but not limited to, switching to a backup device that the sleep lab has available.

Comfort Assessments: At the end of the sleep study (within two business days) all participants will be asked to complete a comfort questionnaire via phone. This call will

be conducted by the sponsor study staff. This phone call should last less than 10 minutes.

Study participants who complete the overnight sleep study successfully and are interested, will be asked to take part in the two week home use sub study. If the participant agrees to participate, they will receive one on one training on the Vector NIV device and accessories by clinical study staff and/or Philips engineers. They will also be given a device user manual. Once trained on the device, study participants will be asked to take the device home and use as instructed during the night for a 2 week period. Study participants will be given the mask that was used for the overnight sleep study to use with the Vector NIV device for the 2 week period.

-Optional Exit Interview and/or EFL assessment – (within 5 months of visit 1)

Participants may be asked to return to the clinical study site for an optional EFL screening/determination and/or complete an optional open interview. at any time during the study or sub-study. The interview and EFL screening/determination session may be videotaped and used for marketing purposes. Participants will consent to the use of this information for these reasons. During the interview, the participant will be asked to answer a set of questions about their opinions related to their experience with the device in the study. This interview will be conducted by a member of the study staff or study sponsor representative. The interview will require up to an hour of the participant's time. Participants will be asked to indicate their approval to the interview and EFL screening/determination session video recorded prior to being scheduled to come into the clinical study site.

**Unscheduled Visits:**

Participants may be asked to participate in this overnight data collection study up to three (3) times. This will occur within a month of the first overnight.

**Vector Home Use Sub Study**

Those participants that successfully completed overnight PSG visits or new participants who are currently using a PAP or NIV device at home will be contacted to participate in a Sub Study involving overnight home use of the Vector NIV device.

Sub- Study Primary Objective:

To evaluate the performance of the Vector NIV device at home for 2 weeks in patients with COPD patients that have been identified as having EFL.

Sub-Study Endpoints:

- Ventilator adherence during 2 week home use sub-study.

- Ventilator-collected parameters during 2 week home use sub-study such as: Mean EPAP, Respiratory Rate, Minute Ventilation, and ΔXrs values
- Patient Therapy Comfort assessment via Questionnaires

Additional Inclusion/Exclusion Criteria:

Inclusion Criteria:

1. Participants who completed the initial study and who would be willing to use the Vector NIV device at home during the night for a 2 week period ***OR***
2. Participants prescribed and currently using a PAP or NIV device at home who meet study inclusion/exclusion criteria of primary protocol

Exclusion Criteria

1. Participants currently using a PAP or NIV device at home with a documented EPAP setting on their current device that is greater than then the mean or final EPAP determined during the therapy session of the screening visit.

Sub-Study Schedule of Events:

Sub-Study Screening Visit:

- All study participants will undergo the exact same study procedures as in study visit 1 in the primary study with the following differences:
    1. Study participants who are currently using an NIV or PAP therapy device at home that have a EPAP setting that is greater than the mean or final EPAP determined during the 20 minute therapy session will not be asked to continue onto the 2 week device home use period.
    2. Participants who are currently on NIV or PAP will not be scheduled for an overnight PSG.
    3. Once eligibility has been confirmed, participants will receive one on one training on the Vector NIV device and accessories by clinical study staff. They will also be given a device user manual. Once trained on the device, study participants will be asked to take the device home and use as instructed during the night for a 2 week period.

Sub-Study Office Visit:

- At the end of the 2 week device home use period, study participants will be asked to return to the clinical study site to return the study Vector NIV device and complete a survey.

Unscheduled Sub-Study Visits:

Participants may be asked to repeat the two week take home portion of the study up to three (3) times. This will occur within three months of the sub-study screening visit.

# Selection and Withdrawal of Subjects:

**Inclusion Criteria**

1. Age ≥ 40 years of age; ≤ 80 years of age
2. Ability to provide consent
3. Diagnosis of COPD
4. Must present with EFL via screening of the vector device at 3 cmH2O
5. Have an EPAP to abolish EFL greater or equal to 6cmH2O
6. Must be able to maintain SpO2 greater than 88% at rest and during EPAP Titration

**Exclusion Criteria:**

1. Any major non COPD uncontrolled disease or condition, such as congestive heart failure, malignancy, liver or renal insufficiency (that requires current evaluation for liver or renal transplantation or dialysis), amyotrophic lateral sclerosis, or severe stroke, or other condition as deemed appropriate by investigator as determined by review of medical history and / or participant reported medical history
2. Suffering from a COPD exacerbation at the time of data collection or in the 30 days prior to data collection
3. Self-reported Pregnancy
4. Employee or family member that is affiliated with Philips Respironics
5. Currently employed by a manufacturer of respiratory products or family member employed by a manufacturer of respiratory products
6. History of bullous emphysema
7. History of pneumothorax
8. Evidence of acute sinusitis or otitis media
9. Hypotension
10. Participants at risk for aspiration of gastric contents
11. Epistaxis
12. Participants in respiratory failure
13. Inability to maintain a patent airway or adequately clear secretions

**Withdrawal:**

The term "discontinuation" refers to the participant's premature withdrawal from the study prior to completing all procedures. Participants may be discontinued from the study for any of the following reasons:

- If in the investigator's judgement, continuation in the study may prove harmful to the participant. Such a decision may be precipitated by adverse events, including fever, nausea, rash, changes in vital signs, or the development of a new medical condition. The investigator will be solely responsible for making medical/safety decisions regarding the participant's continued participation in the study.
- Noncompliance
- At the request of the participant.

The study team will document whether or not each participant completed the study. If, for any participant, study treatment or assessments were discontinued, the reason will be recorded.

The study goal is to have up to 20 participants successfully complete the study.

# Treatment of Subjects:

**Intended Use**

The Vector ventilator is intended to provide non-invasive ventilatory support to treat adult patients with Respiratory Insufficiency with primary cause being COPD. It is intended to be used within the home, institution/hospital, and diagnostic laboratory environments. This device is not intended for life support. It can be used to screen for the presence, and abolishment of Expiratory Flow

**Limitations/Contraindications:**

- Existing respiratory failure
- Acute sinusitis, otitis media
- Hypotension
- At risk for aspiration of gastric contents
- Epistaxis, causing pulmonary aspiration of blood
- Inability to maintain a patent airway or adequately clear secretions

**Monitoring:**

This clinical study will be monitored by Philips Respironics Inc. (Sponsor) in compliance with the Code of Federal Regulations (CFR) for clinical research; namely, 21 CFR Parts 50, 54, 56 and 812 and others as applicable. The purpose of such monitoring is to assure that the study remains in compliance with the approved protocol, investigator agreement and regulatory

requirements, to verify the completeness, reliability and accuracy of study data and to resolve any issues that arise during the conduction of the study. The Sponsor will conduct monitoring visits periodically as specified by the monitoring plan. Monitoring will be conduct by trained clinical research professionals.

It has been determined that this study does not require a Data Safety Monitoring Board (DSMB).

# Assessment of Performance

Device performance will be based on the following recorded Ventilator parameters:

- Mean EPAP, Respiratory Rate, Minute Ventilation, and ΔXrs values
- Ventilator collected parameters during the EFL screening; ΔXrs value, % flow limited breaths, & mask leak values

# Assessment of Safety

All serious adverse events, occurring during the course of the study will be collected, fully documented, and reported to the Institutional Internal Review Board by the site Principal Investigator, or sponsor staff. Serious adverse events will be reviewed by the Sponsor within 24 hours of the study team being aware of the event.

All adverse events will be collected and reviewed. As any events will be reported electronically or directly from a person the study team will collect the onset, duration, intensity and treatment required, outcome and action taken. In addition to adverse event reporting, the study staff will report a summary of the protocol findings, participant recruitment, drop-outs, and events to the IRB annually.

# Device Deficiencies

All device deficiencies, use or user errors, and equipment failures will be documented. Use or User errors will be captured as part of the source documentation. Device deficiencies and equipment failures will be kept on a separate log. The serial numbers and type of deficiency/failure will be captured. Unanticipated device deficiencies that lead to SAE's will be reviewed with the PI and reported to the IRB as required.

# Statistical Methods

### General Considerations

The purpose of this engineering study is to collect engineering and subjective data on the Vector device. No formal statistical analysis is planned. Any deviations to this approach will be indicated in either a revised protocol or in the study report. Baseline and questionnaire ratings will be summarized with descriptive statistics: continuous data will be presented as averages and standard deviations, and categorical data will be presented as frequencies and percentages.

**Participant Disposition**

Participant disposition, including the total number of participants enrolled, completed, early terminations and withdrawals, will be presented. A listing will be provided with the reasons for discontinuation.

**Safety Analysis**

Safety evaluations will be performed by recording clinical adverse events at the time originally reported as a part of the study visits. Adverse events will be provided in data listings.

**Interim Analysis**

Since this is an engineering evaluation, data will be reviewed during the course of the study, but a formal interim analysis does not apply.

# Direct Access to Source Data / Documents

Only site clinical study staff and approved Philips staff working with the research will know the identity of the participants. All information recorded by the study team and provided for analysis will be given a study ID number.

Privacy rules and requirements according to federal and state governing regulations will be implemented. All the information collected as part of this study will be kept confidential. All information collected for this study will be kept in a secured area or stored in a password protected computer if digital. Except when required by law, participants will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records. For records disclosed to Philips Respironics participants will be assigned a unique code number.

Results of the study related data, medical history, and information obtained from the questionnaire and device data will be reported and received by Philips Respironics. Philips Respironics will use participant study data for research purposes to support engineering objectives described in this protocol.

In addition, participant records may be reviewed in order to meet federal and state regulations. Reviewers may include representatives from the FDA or similar government authorities in other countries where the device is being used, and Philips Respironics for the purposes of the following side effects, and to gather additional information related to the study, and the Institutional Review Board (IRB). Participant permission for review of confidential information is granted by signing the associated informed consent. Philips Respironics will ensure that it follows all applicable state and federal data protection regulations.

**Provisions to Protect the Privacy Interests of Participants:** Participants will only interact with approved members of the research staff, and will have the option to decline

to provide any information that they are uncomfortable revealing. All research staff (site and sponsor) will receive training regarding the protection of human subject data. Participant's medical records will only be accessed after obtaining written consent from the participant, and will only be reviewed by members of the research staff for whom review of this information is necessary for continued participation in the study (e.g. Philips research staff and study investigator reviewing the medical records).

## Case Report Forms

The site study team will capture information on source documents. These source documents will be provided to the sponsor for data analysis. Copies of the source will remain with the site. Only staff delegated by the PI will have the ability to enter in, or make changes to, the source documents. Data from source documents will be entered into spreadsheet by a Philips representative and will be monitored according to monitoring plan. All data collected by the sponsor collected and maintained by the sponsor, will be kept confidential, and stored in a secure location if on paper or on a secure server or protected device.

## Quality Control and Quality Assurance

The PI and study personnel will be trained to the study protocol, study product, TMF documents, monitoring plan, CRFs and/or eCRFs, direct data reporting, and all Sponsor expectations, as applicable. Once complete, training and delegations will be documented for PI and study personnel.

Data queries will be addressed by delegated study personnel and CRF/ eCRFs will be reviewed and signed off by PI prior to study closure. Monitoring will be completed in accordance with US FDA CFR, as applicable.

## Ethics

This study will be submitted and reviewed by the Allendale Review Board. All participants will be consented prior to completing the trial. The Primary Investigator will review all adverse events as it relates to the study device.

This study will receive approval and oversight from
Allendale Institutional Review Board
30 Neck Road
Old Lyme, Connecticut
United States
(860) 434-5872

All data will be kept confidential and in a secure location if on paper or on a secure server or device. Only approved study personnel will have access to study related

documents. All electronic data shall be stored in a coded data set. All paper documents shall be kept in a secure area. Study data and source will be made available for study related monitoring or audits by the IRB/IEC, sponsor, or regulatory inspection(s). Results of the study related data, and information obtained from the engineering study, will be collected, received and reported by Philips Respironics. Philips Respironics will use participant study data for research purposes to support scientific and marketing objectives described in this protocol.

# Data Handling and Recordkeeping

Hard copies of the study will be kept on site for at least 2 years after study completion. The sponsor will maintain study records indefinitely. Records will be stored at Iron Mountain, a secure information management services company.

# Financing and Insurance

If the participant is injured during the course of the trial and as a direct result of this trial, they should contact the Principal Investigator, William Sims, MD. The participant will be directed to seek clinically appropriate medical care for that injury. However, we cannot guarantee that the medical care and treatment will be provided without charge or that it will be paid for by the participants insurance company, and the costs incurred may ultimately be the participant's responsibility.

# Registration on ClinicalTrials.gov or other applicable registry

As this is engineering clinical evaluation, this will not be registered on ClinicalTrials.gov or other applicable registry.

# Risk and Benefit Analysis

## Potential Risks and Discomforts

This is a minimal risk study. Potential risks are detailed below and will be listed in the ICF and discussed during the consenting process.

The risks of providing noninvasive ventilation with the Vector NIV device are no greater than the risks encountered with other assisted positive airway pressure (PAP) devices. There are no significant risks will be posed to the participants participating in this protocol, as the device is a non-significant risk device and the study is non-invasive and will be conducted in a sleep lab and monitored by a trained clinical staff as well as Philips Respironics engineer. The equipment has been tested to ensure safety. Should the equipment not perform as designed, therapy could increase and / or decrease more than desired. This affect could be uncomfortable or awaken the participant.

A trained clinician will be present monitoring the participant while the device is in use the sleep lab. The clinician will intervene should any problems be identified. One possible intervention could be for the clinician to stop the study in the event that participant's oxygen saturation ($SpO_2$) falls below 88%. The participant can also easily remove their interface device should it become uncomfortable or make breathing difficult. Other potential side effects of PAP therapy may include: ear discomfort, conjunctivitis, skin abrasions due to non-invasive interfaces and gastric distension (aerophagia), all of which are quite uncommon. Thus, we believe that the risks and discomfort are minimal. All masks used for this study are commercially available products.

Oxygen saturations ($SpO_2$) will be monitored throughout the duration of the nocturnal study.

The patient may sleep poorly during the nocturnal sleep study and thus may be sleepy the next day. If the patient is too sleepy to drive home, other forms of transportation will be utilized.

Should any problems be identified during the 2 week home use period, participants can easily remove their mask interface during the night and discontinue use of the Study Vector NIV device. Those study participants who are on existing PAP or NIV therapy will be instructed to resume use with their current device.

## Potential Benefits

Although participation in this trial will not result in any direct benefit to the subject, they will be contributing to generalizable data that will help improve device design and function.

## Compensation for Research-Related Activities

Participants will only be compensated for the activities that they complete. Participants' payment will be maded according to the following schedule.

| Activity | Payment Amount | Payment Timing |
|---|---|---|
| Screening Visit | $50 | Within 6 weeks after visit |
| Overnight Sleep study visit | $200 | Within 6 weeks after visit |
| Optional Exit Interview visit | $50 | Within 6 weeks after visit |
| SubStudy Visit 1 | $50 | Within 6 weeks after visit |
| 2 week take home | $50/week | Within 6 weeks after visit |
| Completion of SubStudy Exit Interview | $50 | Within 6 weeks after visit |

## Publication

At this time, there are no planned publication submissions for this study.

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