Clinical Protocol

Feasibility Study of a Mask Adhesive in Patients Treated with NIV in an Institutional Setting

Version 2.0
FINAL

Protocol ID: SRC_HRC_Mask Adhesive (MANIV Trial)_2020_11130

21 APR 2020

Amendment 1

Sponsored By

Philips RS North America LLC f/k/a Respironics, Inc.
6501 Living Place
Pittsburgh, PA 15206

Sponsor Approval

[redacted]

Author Signature Date

[redacted]

Author Signature Date

[redacted]

Author Signature Date

Investigator Signature Page

As Investigator of the study entitled "Feasibility Study of a Mask Adhesive in Patients Treated with NIV in an Institutional Setting" Protocol ID: SRC_HRC_Mask Adhesive (MANIV Trial)_2020_11130, 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 Philips (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: [redacted] **Date**: [redacted]

Printed Name: [redacted]

Table of Contents

Document Control Page(s)

Protocol Title: Feasibility Study of a Mask Adhesive in Patients Treated with NIV in an Institutional Setting

Protocol ID: SRC_HRC_Mask Adhesive (MANIV Trial)_2020_11130

Protocol Version: 2.0

Version Date: 21 APR 2021

Author(s): Beth Galaska, MID; Jeff Jasko, MS; Melissa Weiner, MPH

Study Sponsor:

Respironics California, LLC
Hospital Respiratory Care
2271 Cosmos Ct
Carlsbad, CA 92011

Sponsor Contact Information

Sponsor Contact Information

Study Monitor:

Melissa Weiner
Clinical Research Associate
[redacted]

Reporting of Adverse Events or Adverse Device Effects

Report the occurrence of a serious adverse events, serious adverse device effects, or unanticipated adverse device effects to Philips within 24 hours of the occurrence.

Melissa Weiner
Clinical Research Associate
[redacted]

1. PROTOCOL SYNOPSIS

Title:	Feasibility Study of a Mask Adhesive in Patients Treated with NIV in an Institutional Setting
Study Design:	Randomized, Open-Label, Crossover Study
Objectives:	Primary Objectives: • To determine the incidence of severe medical adhesive-related skin injury (MARSI) when used in an institutional setting • To evaluate the mask adhesive ease-of-use in an institutional setting Secondary Objective: • To evaluate the performance of the mask adhesive in reducing leaks in an institutional setting
Endpoints:	Primary Endpoints: • Proportion of patients who have severe and extreme skin irritation that persists for ≥ 30 min after mask adhesive removal (score of ≥ 3 on a 5-point grading system) • Clinician-perceived mask adhesive ease-of-use as measured by a 0-10 Likert Scale (initial impressions/end of study) Secondary Endpoint: • Leak reduction. Calculated percentage change in unintentional leak volume (L/min) after mask adhesive use as compared to the use of the mask without the adhesive
Study Population:	• Up to 30 adult patients treated with NIV will be enrolled in this study • Up to 30 clinicians at each site who treat patients during this study
Description the Accessory to be tested:	The Philips mask adhesive is an optional accessory to the AF531 or PerformaTrak masks. It is a double-sided adhesive, with one side applied directly to the patient's skin and the other side connected to the mask cushion. The adhesive is only to be applied to a patient once. The mask cushion side can be removed from the adhesive and then re-applied, as necessary. For example, if the patient needs

	to remove the mask to eat or take medicine, the mask is removed from the patient and the adhesive will stay on the patient's face.
Study Duration:	Estimated 9 month accrual and follow-up period.
Participant Duration:	Participant study duration will be a maximum of 5 business days, with 2 nights of planned intervention and ~8 hours of adhesive mask use.

2. Background Information

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by the novel coronavirus (nCoV) which has spread rapidly around the world.[1]

Approximately 14% people with COVID-19 develop severe disease that requires hospitalization and oxygen support, and 5% require intensive care and can be complicated by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia.[2] It has been reported that 19% of the patients with COVID -19 experience hypoxic respiratory failure[3] requiring ventilatory support such as high-flow nasal oxygen (HFNO), invasive and noninvasive ventilation (NIV).

NIV refers to the delivery of positive pressure ventilation through an interface such as nasal mask, face mask, or a helmet and it is recommended as a treatment for patients with mild-to-moderate acute respiratory failure.[4]

Although effectiveness on improving survival NIV has been supported by several randomized trials,[5] there is a concern with the use NIV in patients with respiratory tract infection due to the potential respirable aerosol (droplet size < 5 μm) and larger droplet (> 10 μm) spread as the mode of transmissible infections.[6,7] It is recognized that unintentional leaks and poor fitting of the NIV interface[8] increase the risk of spreading droplets that might carry contaminating viruses, increasing the risk of spreading the disease to other patients and health care workers.[9]

To reduce interface leak and aerosol spread, Philips has developed an accessory to non-invasive ventilation masks to be used with the Philips AF531 and the PerformaTrak mask. For the purposes of capturing initial mask leak and safety data, this study will enroll patients treated with NIV in an institutional setting (i.e., sleep lab).

3. Description of the Study Product

The Mask Adhesive serves as an accessory to the AF531/PerformaTrak masks with the intent to reduce patient leak while a patient is receiving therapy. This accessory is a double-sided adhesive; with one side applied directly to the patient's skin and the other side connected to the mask cushion. Each adhesive is only to be applied to a patient once. The AF531/Performatrak mask can be removed from the adhesive and then re-applied, as necessary. For example, if the patient needs to remove the mask to eat or take medicine, the mask is removed from the patient and the adhesive will stay on the patient's face. The instructions for use (IFU) state that the adhesive should be replaced as necessary by the caregiver. The material used in the adhesive mask is an acrylic tape, 3M™ Medical Foam Tape 1774T (3M Health Care, St Paul, Minnesota) and it has undergone safety evaluations including in vitro cytototoxicity, MEM Elution, Primary Skin Irritation and Sensitization. All tests were conducted in compliance with the requirements of ISO 10993-5: Biological Evaluation of Medical Devices, Part 5: Tests for In Vitro Cytotoxicity and ISO 10993-10, Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Delayed-Type Hypersensitivity.

Intended Use: The adhesive accessory is intended to secure the mask cushion to the patient's face. The adhesive accessory is for single patient use in the hospital/institutional environment only.

Contraindications: Adhesive is not to be used on patients with a pre-existing allergy to tape or adhesive, existing skin breakdown or wounds, or skin that lacks the integrity to support removal of adhesive without tearing.

Warnings

- Monitor the patient during use of the adhesive and suspend use if the patient is showing any signs of skin breakdown
- Do not apply over current blisters, open skin or pre-existing skin conditions
- The Mask Adhesive is not a replacement for the headgear. Always use the headgear with the mask and Mask Adhesive

4. Study Purpose

The purpose of this feasibility study is to assess skin integrity and to evaluate the ease-of-use of a mask adhesive on individuals who have been prescribed NIV.

5. Study Objectives and Endpoints

Primary	
Objectives	**Endpoints**
• To determine the incidence of severe medical adhesive-related skin injury (MARSI) when used in an institutional setting • To evaluate the mask adhesive ease-of-use in an institutional setting	• Proportion of patients who have severe and extreme skin irritation that persists for ≥ 30 min after mask adhesive removal (score of ≥ 3 on a 5-point grading system) • Clinician-perceived mask adhesive ease-of-use as measured by a 0-10 Likert Scale (initial impressions/end of study)
Secondary	
Objectives	**Endpoints**
• To evaluate the performance of the mask adhesive in reducing leaks in an institutional setting	• Leak reduction. Calculated percentage change in leak volume (L/min) after mask adhesive use as compared to the use of the mask without the adhesive
Exploratory	
Objectives	**Endpoints**
• To evaluate participant's comfort with the mask adhesive	• Proportion of participants who rated comfort with the mask adhesive as 6 or higher (per participant report)
• To determine factors associated with the development of MARSI in patients using the mask adhesive	• Predictors of development of MARSI; include but are not limited to: age, BMI, presence of allergies, underlying medical condition, medications
• To explore changes in patient leak over time with varying pressures when the mask adhesive is in use	• Leak reduction. Calculated percentage change in leak volume (L/min) with mask adhesive use over an extended period

6. Study Design and Rationale

This is a randomized, open-label, crossover study to assess the ease-of-use and performance of a Class I medical device accessory. Participants (patients and clinicians) will undergo the informed consent process and sign an informed consent form (ICF). This study will be completed according to ICH for Good Clinical Practice guidance E6 (R2) Good Clinical Practice, March 2018 and the Declaration of Helsinki. The study will be monitored in accordance with the Study Monitoring Plan.

7. Study Population

7.1 Patients

Up to 30 patients will be enrolled over an estimated nine month accrual and follow-up evaluation period.

Inclusion Criteria

- Adults aged 18 to 85 (inclusive)
- Adults treated with NIV
- Able to read, write, and speak English
- Able to provide written informed consent
- Willing to have facial hair removed for adhesive placement (if required)

Exclusion Criteria

- Pre-existing allergy to tape or adhesive
- Blisters, open skin or pre-existing skin condition that may impact the ability to support removal of the mask adhesive without tearing the skin
- Pregnant (for females of childbearing age)
- Individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing

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 judgment, 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.
- If the mask is found to be inadequate for use (i.e., seal stability, comfort, air flow)
- At the request of the participant.
- At the request of the Study Sponsor, Philips.

The study team will document whether each participant completed the study. Successful study completion will be defined as the placement and removal of at least one mask adhesive. If, for any participant, study treatment or assessments were discontinued, the reason will be recorded. Participants may withdraw from the study at any time. Withdrawal from the study will not affect their medical treatment or future participation in a research study. Participants that withdraw from the study will not be replaced, and no further data will be collected after date of withdrawal.

8. Study Procedures

Participants’ safety

The FDA Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Public Health Emergency will be followed and local procedures will be followed to ensure the safety of study participants, maintain compliance with good clinical practice (GCP), and minimize risks to study integrity for the duration of the COVID-19 public health emergency.

8.1 Patients

Pre-Screening

Potential participants will be pre-screened predominantly through chart review from the existing site databases of patients. All efforts will be made to ensure patient privacy. The study staff will provide verbal explanation regarding the nature of the study via telephone screening. In addition, IRB-approved recruitment materials will be posted and available for distribution at the clinic.

Screening and Enrollment

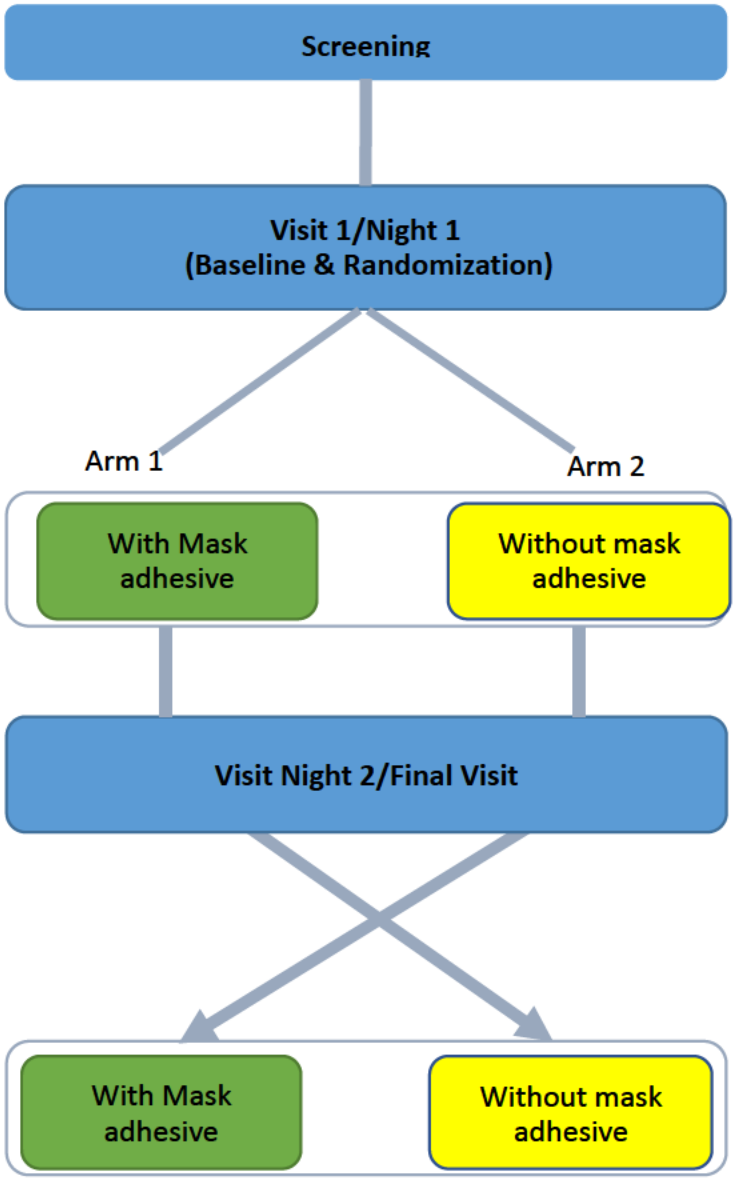
The study will be explained to the patients by qualified site personnel. The patient will be given time to read the consent document and ask any questions that they might have. Individuals who agree to participate will be asked to sign the consent form. Eligibility will be assessed following informed consent. If the participant is found to be ineligible, all study procedures will stop and the participants will be considered a screen fail.

Baseline Data Collection

After the patient provides informed consent and eligibility has been assessed, the following patient information will be reviewed and collected via participant self-report:

- Demographics including, e.g. age, race, ethnicity, gender, etc.
- Anthropometric data, e.g., height and weight, etc.
- Relevant medical history, current NIV therapy (i.e., settings, mask, duration of BiPAP use, etc.) including any known allergies to acrylic tape or adhesive
- Concurrent medications
- Baseline facial skin assessment to evaluate skin breakdown or wounds, or skin that lacks the integrity to support removal of adhesive without tearing, dental assessment, etc.

Randomization. Participants will be randomly allocated to the order of mask use. Participants allocated to study arm 1 will use the mask with the mask adhesive on the first study night and the mask only on the second study night. Participants allocated to study arm 2 will use the mask only on the first study night, and the mask with the mask adhesive on the second study night.



Night 1 & Night 2

Prior to Mask Application:

- Vital signs, including heart rate, respiratory, blood pressure, peripheral capillary oxygen saturation (SpO2)
    - Optional (when available)
        - End Tidal Carbon Dioxide (EtCO2)
- Time/Date of mask adhesive application (mask adhesive arm only)
- NIV therapy information:
    - Device brand name, model

- Device Settings and leak
- Mask information: AF531 or PerformaTrak, and mask size

Facial Skin Assessment:

- A 5-point MARSI grading scale will be used to evaluate erythema/edema. The scale will be as follows:
  - 0=No redness
  - 1=Slight redness, barely perceptible
  - 2=Definite redness
  - 3=Severe redness (well defined) with edema
  - 4=Extreme response with edema (swelling)

Mask adhesive placement Before the night when the mask adhesive will be used, clinicians will follow the instructions for use and the product identification number will be recorded.

After mask application and initiation of the BiPAP therapy, the following parameters will be recorded after patient stabilization:

- Mask information: AF531 or PerformaTrak, mask size
- Vent Settings/Information (personal or site provided with standard of care therapy):
  - Device brand name, model
  - Time/Date of NIV initiation
  - Settings and leak
- SpO_2 levels
- $EtCO_2$ (when available)

Overnight Procedure

The participants will be monitored continuously during the night by a trained sleep technologist, including standard of care measures, ECG, SPO2, etc.

Leak, O_2 levels and $EtCO_2$ (when available) will be recorded.

After the Overnight study

Skin Evaluation

Mask adhesive condition, i.e. peeling, soiled, etc., and skin status will be evaluated and recorded following approximately after 8 hours of use of the mask adhesive (i.e. mask and mask adhesive arm). Skin status will be evaluated and recorded (i.e. mask without mask adhesive arm) and/or upon mask removal. The abovementioned 5-point MARSI grading scale will be used to evaluate erythema/edema (approximately 30 minutes after mask adhesive is removed).

Leak, O_2 levels and $EtCO_2$ (when available) will also be recorded. Per local practice, and only with participant opt-in consent, site(s) may photograph participants' faces to document skin condition.

8.2 Clinicians

Ease-of-use data will be collected from clinicians who have used the mask adhesive. It is preferred that the clinicians apply the mask at least two times before completing the questionnaire and then repeat the questionnaire at the end of study.

Table 1 Study Procedures Summary (Sleep Patients Only)

Procedure	Visit 1/ Baseline	Visit 1/ Night 1	Visit 2/ Night 2
Pre-Screen Potential Participants	**Pre-Study**		
Informed Consent	**X**		
Assess eligibility (Inclusion/Exclusion)	**X**		
Assign PTID	**X**		
Medical History (to include comorbidities), Baseline Medical Condition, Dental Assessment, Demographics	**X**		
Concomitant Meds	**X**		
Randomization	**X**		
Vent settings		**X**	**X**

Procedure	Visit 1/ Baseline	Visit 1/ Night 1	Visit 2/ Night 2
Participant questionnaire Mask Acceptability	X		X
Product usage form, to include mask adhesive (peeling, soiled, etc.) assessment		X	X
Skin assessment	X	X (Pre and Post Application)	X (Pre and Post Application)
ECG for Safety Only (not captured in EDC)		X	X
O2 levels	X	X	X
EtCO2 (when available)	X	X	X
Unintentional leak measurement before mask placement		X	X
Unintentional leak measurement after mask placement		X	X
Ventilator Device Log Data (when available)		X	X
Study product dispensation and documentation		X	X
Side effects/AE Monitoring		X	X
Study Discontinuation	*	*	X

**If indicated*

Study Duration

The total duration of the study is expected to be nine months for accrual and follow-up. Patient participants will be enrolled for up to five business days. However, time on the study will not exceed 2 nights.

9. Statistical Methods

Determination of Sample Size

No sample-size calculation was performed for this feasibility study. The results of this study may be used to power a subsequent trial.

General Considerations

Descriptive statistics will be presented for all variables of interest. Continuous data will be summarized by mean, standard deviation, median, minimum, and maximum values, and 95%

confidence interval, effect size, and number of observations. Categorical data will be presented as frequencies, percentages and 95% Clopper-Pearson confidence intervals. Any formal significance testing will be performed at $p < 0.05$. There are no statistical criteria for terminating the study and any deviations from the original statistical plan will be noted in the analysis report.

Primary Analysis

Incidence of Severe Medical Adhesive-Related Skin Injury

Patients who have severe and extreme skin irritation that persists for ≥ 30 min after mask adhesive removal (score of ≥ 3 on the 5-point grading system) will be summarized by percentage and frequency of occurrence. The results will also be presented with a 95% Clopper-Pearson confidence interval.

Mask Adhesive Ease-of-Use

The clinician-reported ease-of-use ratings will be inspected for normality. Depending on the distributions of the data, a paired t-test or Wilcoxon Signed-Ranks test will examine whether the average (or median) score is greater than 5. This will be tested both on the initial-impression and end-of-study ratings, with Sidak adjustment to account for multiple comparisons. In addition, a paired t-test or Wilcoxon Signed-Ranks test will examine whether there is a significant change in ratings between these two intervals [end of study] – [initial impression].

Secondary Analysis

Leak Reduction

Percentage change in leak will be calculated as ([Leak with the mask adhesive applied] – [Leak without the mask adhesive])/[Leak without the mask adhesive]. The percentage change will be examined using either a paired t-test or the nonparametric Wilcoxon Signed-Ranks test, depending on the distribution of the data. Sub-group analysis will be performed to explore the impact of differing dental conditions.

Exploratory Analysis

Mask Adhesive Participant Comfort

The participant-reported comfort ratings will be inspected for normality. Depending on the distributions of the data, a paired t-test or Wilcoxon Signed-Ranks test will examine whether the average (or median) score is greater than 5.

Factors Associated with the Development of MARSI and Patient Leak Data Captured Over Time

If adequate data are collected, an exploratory analysis may be performed. The details of this analysis would be described in the study report.

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.

Subject Accountability and Missing Data

Participants who withdraw from the study will be tabulated with the reasons for the withdrawal. It is not anticipated that imputation methods will be required.

Safety Analysis

All reportable adverse events (serious and non-serious) that occur during the study will be documented on the Adverse Event form or eCRF, and the data will be provided in listings.

Interim Analysis

No interim analysis is planned.

10. Direct Access to Source Data/Documents

As part of the study, the study team will record information that contains the participants' name and other personal identifiers. Study records that identify participants will be kept confidential, as required by law. Federal Privacy Regulations require us to safeguard participant information including implementing privacy and security safeguards to prevent unauthorized access to

records. Except when required by law, name, social security number, address, telephone number, or any other direct personal identifiers in study records disclosed outside of the research site will not identify participants. Records of participants will be assigned a unique code number. The key to the code will be kept separately, will be secured and is only made available to specific study staff.

Results of the study related data and information obtained from the questionnaires will be reported to Philips. Philips will use participant study data for research purposes to support the scientific objectives described in this document. 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 for the purposes of following side effects and gathering additional information related to the study. If a participant's research record is reviewed by any of these groups, information used and disclosed may include the entire research record and clinical and research observations made during participation in the research study. Participant permission for review of confidential information is granted by signing the associated consent form. Philips will ensure that it follows all applicable state and federal data protection regulations.

The study results will be retained for two years; however, the coded data will be retained indefinitely. The Sponsor will use and disclose participant study information only for research or regulatory purposes or to prepare research publications or presentations at meetings.

Clinical study records will be maintained in a site study binder and will be stored in locked cabinets under the control of the Principal Investigator. Electronic data collected will be stored in an access controlled secured database indefinitely. No patient identifying information will be stored in the electronic data capture and no patient identifying information will be used in any reports, meeting presentations, or publications of this study.

The data collected during this study may be reanalyzed at a later date and may be combined with the results of other studies. Philips and those approved by Philips may use the results of this study for other research purposes, including:

1. Reviewing the safety or effectiveness of the study device and other products or therapies;
2. Evaluating other products or therapies for patients;
3. Developing a better understanding of disease

A protocol deviation is any noncompliance with the clinical study protocol. Noncompliance may be either on the part of the participant, the Investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.
It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within five working days of identification of the protocol deviation, or within five working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents and reported to the Sponsor. All deviations are to be documented on the provided protocol deviation log.

11. Adverse Events Handling and Reporting

This study is a preliminary feasibility study of a cleared medical device accessory.
Unanticipated and anticipated adverse events will be recorded if they are definitely, probably, or possibly related to the investigational device as determined by principal Investigator or designee. All events captured will be reported to the Sponsor by the research staff; however, all SAEs, SADEs, UADEs must be reported to the Sponsor within 24 hours of discovering the occurrence of the SAE. The research staff is required to complete and submit the Sponsor's standard SAE form detailing the event. AE's and SAE's will be reported to the IRB per their policy.

<u>Relationship to Study Intervention</u>
All adverse events (AEs) must have their relationship to study intervention initially assessed by the clinician or designee. The Principal Investigator (PI) will examine and confirm the temporal relationship based on his/her clinical judgment. The degree of certainty about causality will be

graded using the categories below. In a clinical study, the device under investigation must always be suspect.

- Definitely Related – An AE is definitely related to study participation if it is clear that the event was caused by study participation. A definitely related event has a strong temporal relationship and an alternative cause is unlikely.
- Probably Related – An AE is probably related when there is a reasonable possibility that the event is likely to have been caused by study participation. The AE has a timely relationship to the study procedure(s) and follows a known pattern of response, but a potential alternative cause may be present.
- Possibly Related – An AE is possibly related when there is a reasonable possibility that the event might have been caused by study participation. A possibly related event may follow no known pattern of response and an alternative cause seems more likely. In other circumstances there may be significant uncertainty about the cause of the event, or a possible relationship to study participation cannot reasonably be ruled out.
- Unrelated/Not Related – The cause of the AE is known and the event is in no way related to any aspect of study participation. If there is any uncertainty regarding AE causality then the event must be assessed as possibly related to research participation and reported to the IRB as indicated. Often, the cause of an unrelated AE is disease progression

An adverse event or device deficiency that does not meet the definition of reportable does not require reporting to the Sponsor (or the eCRFs), unless the approving IRB/EC, regulatory authority requires reporting. An Investigator may opt to report any safety event that does not meet any of the above if thought to be clinically relevant to product use. All reportable AEs deemed to be related study product will be followed clinically until the AE resolves (returns to baseline) or stabilizes.

The disposition of all safety events, assignment of relatedness, and seriousness is the responsibility of the Principal Investigator.

All reportable adverse events will be reported in an interim or final report of the clinical study.

Expedited Reporting

Any SAE, SADE, UADE and will be reported to the Sponsor within 24 hours of the study staff learning of the event:

Melissa Weiner
Clinical Research Associate
[redacted]

Promptly thereafter, the study staff will provide a detailed written report that includes at minimum, the requirements for issuing a complaint. Additionally, upon Philips' request, the Investigator will provide further information related to the safety reporting of a particular event.

The Sponsor will report any unanticipated adverse device effect (regardless of seriousness) to the IRB within 5 days of becoming aware of the event. Additionally, the Sponsor, in conjunction with the service location and Investigator, will report to regulatory authorities as required by national regulations.

12. Device Deficiencies

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 or may lead to an SAE will be reported to the Sponsor within 24 hours of learning of the event.

13. Case Report Forms

Study data will be collected on paper or electronically. Case report forms will include information regarding participant eligibility, performed study procedures, protocol deviations, device deficiencies, and AEs. Data collection is the responsibility of the clinical trial staff. The clinical trial staff is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Only those staff that have been delegated by the PI will be able to enter or make changes to the data in the case report forms

14. Quality Control and Quality Assurance

Training

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 (see associated task), and all Sponsor expectations, as applicable. Once complete, training and delegations will be documented for PI and study personnel.

Monitoring and Monitoring Plan

Remote monitoring visits will be performed periodically and will be conducted by trained clinical research professionals. The monitoring process includes initial site qualifications, site initiations visit, monitoring visits, contact with site staff, and a close-out visit. Study monitoring will be conducted in accordance with the study monitoring plan.

Data Management System

Datatrak

As specified in the Data Management Plan, all data will be entered into DataTrak, a 21 CFR Part 11-compliant data capture system provided by the Sponsor. The data will be housed within a secure server (based in Virginia, USA) and accessible only to the Sponsor, study personnel, and investigators. Access to the Electronic Data Capture (EDC) system will be secured through login/password control managed by a system administrator and appropriated training will be provided. The EDC system provides the capability to perform data management activities within a consistent, auditable, and integrated electronic environment (data security, data entry, data validation). Data entries and modifications will be recorded via an audit trail. If the data manager or study monitors identify data errors or inconsistencies, they will generate queries that will be sent to the Principal Investigators and study staff. After queries are resolved, the database will be locked, and the data will be imported into a statistical software and analyzed by biostatisticians.

15. Ethics

The study and any subject facing materials will be reviewed by an Institutional Review Board (IRB) and the study will not begin until approval has been received by the IRB.

Privacy rules and requirements according to 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 outside Sponsor, participants will be assigned a unique code number. The key to the code will be kept by the Investigator. Data will be managed by study number and analyzed anonymously.
A unique source record will be available for each study participant including documentation of the informed consent form review process, HIPAA completion to ensure patient privacy (United States), if applicable, medical history, and concomitant medications review.

16. Data Handling and Recordkeeping

The site study binder will be kept on site for at least 2 years after study completion. The Sponsor will maintain the Trial Master File as defined by Philips retention policies. Records will be stored a secure information management services company.

17. Benefit/Risk Assessment

Reducing the leak from the mask will potentially lead to the following benefits.

1) The adhesive may reduce leak thereby reducing the amount of air leaking from the patient into the room and that will help to reduce the risk of transmission of COVID-19 and other transmittable disease. The reduction in the risk of transmission of COVID-19 may also reduce the fear of the healthcare providers. This may increase the time they can spend with patients.

2) The Adhesive may reduce the probability of overtightening the headgear and that will reduce the probability of pressure sores that occur over time.

3) The availability of a mask with minimal leak might encourage earlier extubation (to noninvasive ventilation) and thus reduce length of intubation.

The addition of the adhesive accessory has raised the initial probability of harm for Skin abrasion due to removal of adhesive. The following control measures have been implemented:

- Design control measure –The design and application will limit the removal of the adhesive to the patient to one time. When the mask is removed from the patient the cushion will be removed from the adhesive and the adhesive will remain on the patient. This will limit the number of times the adhesive is applied and removed from the patient's skin.
- Labeling control measure –Contraindication – Adhesive is not to be used on patients with a pre-existing allergy to tape or adhesive, existing skin breakdown, wounds and skin that lacks the integrity to support removal of adhesive without tearing.
- Labeling control measure –Warning – Monitor the patient during use of the adhesive and suspend use if the patient is showing any signs of skin breakdown.
- COVID-19 is a risk with any in-person activity, but safety precautions, such as screening, disinfection of study materials, and other site safety measures, will be taken to minimize your risk.

The benefit/risk analysis (ER 2239807) conducted as part of the risk management process concludes that based on the risk mitigations in place, the probability of potential harm is reasonably low and the benefits of the new accessory outweighs the potential risk.

18. Product Accountability

Sites will document lot/batch number upon receipt.

19. Registration on ClinicalTrials.gov or Other Applicable Registry

This trial will be registered on ClinicalTrials.gov as this clinical study is intended for publication in a scientific journal.

20. Publication

Study data and results may be used/considered for submission to a peer-reviewed publication, white paper or scientific abstract.

References

1. WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (nCoV) infection is suspected: interim guidance. 2020.
2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory medicine.* 2020;8(5):475-481.
3. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA.* 2020;323(13):1239-1242.
4. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *The European respiratory journal.* 2017;50(2).
5. Cabrini L, Landoni G, Oriani A, et al. Noninvasive ventilation and survival in acute care settings: a comprehensive systematic review and metaanalysis of randomized controlled trials. *Critical care medicine.* 2015;43(4):880-888.
6. Tellier R, Li Y, Cowling BJ, Tang JW. Recognition of aerosol transmission of infectious agents: a commentary. *BMC infectious diseases.* 2019;19(1):101.
7. Cabrini L, Landoni G, Zangrillo A. Minimise nosocomial spread of 2019-nCoV when treating acute respiratory failure. *Lancet (London, England).* 2020;395(10225):685.
8. Murthy S, Gomersall CD, Fowler RA. Care for Critically Ill Patients With COVID-19. *JAMA.* 2020;323(15):1499-1500.
9. Otero DP, Domínguez DV, Fernández LH, et al. Preventing facial pressure ulcers in patients under non-invasive mechanical ventilation: a randomised control trial. *Journal of wound care.* 2017;26(3):128-136.

Appendices

Appendix 1: Instructions for Use (IFU)

Appendix 2: Ease of Use Questionnaire for Clinicians

Appendix 3: Participant Trial Survey

Document Revision History

Version	Date	Authors	Description of Change	Reason for Change
1.0	2 NOV 2020	FSK, BG, JJ	N/A	N/A
2.0	21 APR 2021	BG, JJ, MW	Study personnel update, extension of the duration of accrual, clarification to participants' duration of trial participation update to the possible collection of photographs for skin evaluation, registration on clinicaltrials.gov and submission to peer-reviewed publications, administrative changes.	Full Version Amendment.