Diagnostic validation of the DreamKit device against polysomnography

Protocol ID: SRC_SLE_Sparkle_PSG_2020_10908

Version 5

26th of July, 2021

Final

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VERSION HISTORY

Version No.	Amendment No.	Version Date	Summary of Changes	Rationale
1.0	N/A	3 Nov 2020	Initial release	N/A
2	1	2 Dec 2020	Clarified purpose of actigraphy Removed waiver of consent request.	IRB request
3	2	15 Jan 2020	Clarification of AE surveillance	Unnecessary for low-risk procedures
4	3	8 Jun 2021	Increased sample size	Needed to allow for additional screening
5	4	26Jul2021	Addition of another clinical site and changes in Philips's staffing	Needed for study completion

SPONSOR SIGN-OFF

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ABBREVIATIONS

Abbreviation	Definition
AASM	American Academy of Sleep Medicine
AE	Adverse event
AHI	Apnea-hypopnea index
CAI	Central apnea index
CFR	Code of Federal Regulations
CI	Confidence interval
CRF	Case report form
CSA	Central sleep apnea
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
FDA	Food and Drug Administration
HSAT	Home sleep apnea test
ICC	Intraclass correlation coefficient
ICH GCP	International Conference on Harmonization Good Clinical Practice
IRB	Institutional review board
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnea
PAP	Positive airway pressure
PARE	Plethysmography-acquired respiratory effort
PSG	Polysomnography
REI	Respiratory event index
RIP	Respiratory inductance plethysmography

RPSGT	Registered polysomnographic technologist
SADE	Serious adverse device event
SAE	Serious adverse event
SDB	Sleep-disordered breathing
SpO_2	Oxygen saturation
STARD	Standards for Reporting Diagnostic Accuracy
UADE	Unanticipated adverse device event
UP	Unanticipated problem
US	United States

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1. STATEMENT OF COMPLIANCE

This study will be carried out in accordance with International Conference on Harmonization Good Clinical Practice (ICH GCP) and the following:

United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

The protocol, informed consent form, recruitment materials, and all participant materials will be submitted to the Institutional Review Board (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 in the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent using a previously approved consent form.

2. PROTOCOL SUMMARY

2.1. Synopsis

Study Title & ID:	Diagnostic validation of the DreamKit device against polysomnography SRC_SLE_Sparkle_PSG_2020_10908
Project Name:	Sparkle
Study Design:	Multi-center validation study.
Objective:	The objective of this study is to demonstrate the diagnostic efficacy of the DreamKit device against the gold-standard comparator, polysomnography (PSG), amongst a sample of *n*=200 participants with and without sleep-disordered breathing (SDB).
Endpoints:	Primary Endpoint: The intraclass correlation coefficient (ICC) for absolute agreement between the PSG- apnea hypopnea index (AHI) and DreamKit-AHI. Secondary Endpoint: The ICC for absolute agreement between the PSG- central apnea index (CAI) and DreamKit-CAI.
Hypotheses:	Hypothesis 1 (Primary): We hypothesize that the lower-bound of the ICC 95% confidence interval (CI) between the PSG-AHI and DreamKit-AHI will be ≥0.75, indicating good reliability. Hypothesis 2 (Secondary): We hypothesize that the lower-bound of the ICC 95% CI between the PSG-CAI and DreamKit-CAI will be ≥0.50, indicating moderate reliability.
Study Sample:	Up to *n*=280 participants will be enrolled, in order for *n*=200 participants to complete the study with valid data. Inclusion Criteria: • INCL1: Aged ≥18 years; • INCL2: Fluent in English; • INCL 3: Able to provide informed consent.

	Exclusion Criteria: • EXCL 1: Self-reported habitual sleep duration of <4 hours/night on average ("How many hours sleep do you usually get per night?"); • EXCL 2: Circadian phase disorder, shift work, or any other issue/condition that would, in the opinion of the site investigator, reduce the likelihood of obtaining at least four hours of sleep during the overnight study; • EXCL 3: History of allergic reactions to medical adhesives; • EXCL 4: Skin rash or other dermatological condition that would impact correct placement of the DreamKit device and/or PSG sensors, and/or would be exacerbated by the presence of the device or sensors; • EXCL 5: Presence of a pacemaker; • EXCL 6: Severe medical condition (controlled or uncontrolled) that would impede data collection in the opinion of the site investigator, including the requirement for oxygen therapy; • EXCL 7 [for those currently using overnight therapy]: Unwilling to withdraw from overnight therapy for a single night and/or clinically unsuitable to withdraw from overnight therapy in the opinion of the site investigator, with overnight therapy including but not limited to any form of positive airway pressure (PAP) or ventilation, oral device including mandibular advancement devices or mouthguard for bruxism, nasal dilator strips, and/or positional device; • EXCL 8 [for those currently using overnight therapy]: Considered by the site investigator to be at risk of an adverse event (AE) resulting from hypersomnolence the day after the overnight visit, such as a high-risk occupation including but not limited to a pilot or commercial driver; • EXCL 9: An employee, or family member of an employee, of a company that designs, sells, or manufactures sleep related products (including Philips).

Study Visits Summary & Duration:	Visit 1: Consent, anthropometrics, vital signs, questionnaires. Visit 2: Overnight, attended PSG with simultaneous DreamKit recording.

2.2. Schedule of Activities

Procedures	Performed by	Visit 1 (office visit)	Visit 2 (overnight)
Informed Consent	Principal Investigator or designee	X	
Anthropometrics and vital signs	Study coordinator	X	
Questionnaire battery	Study coordinator	X	
Sleep study	Technologist		X
Data download and transfer	Study coordinator		X
Adverse event (AE) Monitoring	Study coordinator	X	X
Participant compensation & Study Dismissal	Study coordinator		X

3. INTRODUCTION

3.1. Study Rationale

The primary objective of this study is to assess the diagnostic performance of the DreamKit device against the gold-standard comparator, polysomnography (PSG), amongst a sample of *n*=200 participants with and without sleep-disordered breathing (SDB). Data will be used as evidence to support the proposed intended use statement, described in Section 4.4 below.

Please see ER2235417 (Clinical Strategy & Clinical Development Plan Document – Sparkle) for a comprehensive overview of the clinical development plan for this product. This protocol has been designed to address Evidence ID 006 of ER2235417 (Version 2).

3.2. Background

Home sleep apnea test (HSAT) devices are increasingly used to diagnose obstructive sleep apnea (OSA).[1] Potential advantages of taking the diagnostic process from the hospital to the home include reduced cost; increased access; reduced wait times; higher patient turnover; increased patient comfort; and the collection of data that is more representative of a patient's usual sleep. Drawbacks of the HSAT model include the reduced number of signals compared with PSG; reduced patient/provider contact thereby limiting the opportunity for OSA education/support; and increased possibility of configuration error or signal loss leading to the requirement for further testing.[1-3] Research has demonstrated that a lab-based diagnostic approach is not superior to a home-based approach in terms of self-reported daytime sleepiness, quality of life, blood pressure, and subsequent adherence to positive airway pressure (PAP) measured over four weeks.[4] Development of a simpler HSAT device may be beneficial in terms of maximizing the collection of good quality signals, while also increasing ease of use and patient comfort. The DreamKit device has been designed to meet these needs.

The DreamKit is a single-use adhesive patch containing an accelerometer and pulse oximeter, linked to nasal pressure cannulae. From these three sensors, the following signals can be monitored or derived: nasal airflow, blood oxygen saturation (SpO_2), pulse rate, respiratory effort, sleep time, and head position. The adhesive patch containing the pulse oximeter is designed to be placed on the forehead, connected to adhesive nasal pressure cannulae placed over the nasal bridge and directly below the nostrils. Data are stored in the flash memory on the device, and can be uploaded to a computer upon completion of the recording.

4. OBJECTIVES

The objective of this study is to demonstrate the diagnostic efficacy of the DreamKit device against the gold-standard comparator, PSG, amongst a sample of *n*=200 participants with and without SDB.

4.1. Endpoints

Primary Endpoint: The intraclass correlation coefficient (ICC) for absolute agreement between the PSG-apnea-hypopnea index (AHI) and DreamKit-AHI.

Secondary Endpoint: The ICC for absolute agreement between the PSG-central apnea index (CAI) and DreamKit-CAI.

4.2. Hypotheses

Hypothesis 1 (Primary): We hypothesize that the lower-bound of the ICC 95% confidence interval (CI) between the PSG-AHI and DreamKit-AHI will be ≥0.75, indicating good reliability.[5]

Hypothesis 2 (Secondary): We hypothesize that the lower-bound of the ICC 95% CI between the PSG-CAI and DreamKit-CAI will be ≥0.50, indicating moderate reliability.[5]

4.3. Exploratory Analyses

Exploratory analyses will include investigating reliability of the 3% oxygen desaturation index (ODI3%), total respiratory events, total apneas, total hypopneas, total obstructive apneas, total central apneas, and total mixed apneas; agreement of the AHI categorized according to American Academy of Sleep Medicine AASM thresholds for mild/moderate/severe SDB; diagnostic performance metrics at clinically-relevant thresholds of the AHI, CAI, and ODI3%; event-level differentiation of events; and a comparison of signal quality between the DreamKit and PSG. The primary and secondary analyses will adopt the AASM recommended criteria for identifying hypopneas; in exploratory analyses we will also investigate the impact of using the alternative criteria.

4.4. Claims and Intended Performance

The proposed intended use statement for DreamKit is as follows, with the parts relevant to this study bolded (wording may change before regulatory submission):

> *The DreamKit device is a physiologic data recorder intended to collect and record data for use by clinical software used in polysomnography and sleep disorder studies* ***for the diagnosis of sleep related breathing disorders****. The Plethysmography-Acquired Respiratory Effort (PARE) algorithm provides a respiratory effort signal acquired from the DreamKit photoplethysmography signal that correlates with traditional respiratory effort signals used in polysomnography. The DreamKit with PARE provides the information required to* ***detect apneas and hypopneas and classify these***

respiratory events as central, mixed, or obstructive. *It is intended for adult use and can be used in a hospital, clinic, or patient home.*

4.5. Considerations regarding study endpoints

4.5.1. Rationale for the selection of endpoints

The table below summarizes the respiratory parameters required to be reported for HSATs in clinical settings, per the AASM Scoring Manual (Version 2.6). We prioritized the AHI and CAI for our primary and secondary hypotheses, respectively, and included all other listed variables in our exploratory analyses.

Table 1: AASM reporting requirements for adult HSAT reports

Parameter	AASM Reporting Requirement	Endpoint
Respiratory event index* (REI); events/hour	Recommended	Primary (continuous) Exploratory (4-category and binary)
CAI; events/hour	Optional	Secondary (continuous) Exploratory (binary)
Number of respiratory events	Recommended	Exploratory (continuous)
Number of apneas	Recommended	Exploratory (continuous)
Number of hypopneas	Recommended	Exploratory (continuous)
Number of obstructive apneas	Optional	Exploratory (continuous)
Number of central apneas	Optional	Exploratory (continuous)
Number of mixed apneas	Optional	Exploratory (continuous)
A measure of SpO_2 saturation: • ODI3% or ODI4% • SpO_2 Mean/maximum/minimum • Percentage of time <88% or other SpO_2 threshold	Recommended	Exploratory (continuous) [based on ODI3%]

The AASM scoring manual (Version 2.6) Section IX, Part 1, stipulates that recommended parameters must be reported, and that optional parameters may be monitored at the discretion of the clinician or investigator and if monitored, should be reported.

* Throughout this document, we refer to the AHI rather than the REI, as the DreamKit includes a measurement of sleep (see Section 8.1.5).

4.5.2. Rationale for the identification of performance thresholds

We adopted the standards of Koo and Li (2016)[5] and identified a performance target of ≥0.75 for the lower-bound of the 95% CI of the ICC for the AHI, representing good reliability. A meta-analysis of 13 studies representing *n*=853 participants reported agreement between the PSG-AHI and the WatchPAT-AHI, falling into the same category of good reliability (0.893; 95% CI 0.857 – 0.920) (the exact type of correlation coefficient in this paper was not specified).[6]

We identified a performance target of ≥0.50 for the lower-bound of the 95% CI of the ICC for the CAI, representing moderate reliability. In their recent 510(k) submission for the Nox Sleep System (K192469; November 13th, 2019), Nox Medical adopted the same analysis along with a target of 0.46, as has been reported elsewhere in the literature.[7]

Neither the WatchPAT nor Nox Sleep System are the predicate device for DreamKit; however, they are comparable devices with similar intended use statements to the DreamKit, all of which claim to be a diagnostic aid for sleep disorders. The Watch-PAT300 (Itamar Medical; Caesarea, Israel) is an FDA-approved (K153070) HSAT device which uses finger peripheral arterial tonometry, heart rate, and oxygen saturation to identify respiratory events and estimate sleep staging in the compatible zzzPAT software. The Nox Sleep System (Nox Medical; Reykjavik, Iceland) is an FDA-approved (K192469) platform consisting of a HSAT device, PSG device, software, mobile platform, and accessories.

4.6. Inclusion of Actigraphy

For exploratory product development purposes, we will also collect data from a wrist actigraphy device (GENEActiv Original; Activinsights). The actigraphy data will not contribute to any DreamKit analyses. The presence of the actigraphy device is akin to a participant sleeping with a regular wristwatch, and will therefore not impact the data used for the DreamKit analyses.

The safety or efficacy of the actigraphy device is not under investigation. The use of these devices is to collect data for exploratory purposes.

5. STUDY DESIGN

5.1. Overall Design

This is a multi-center study performed for the purpose of diagnostic validation. Up to *n*=280 participants will be enrolled, in order for *n*=200 participants to complete the study with evaluable data. Completion of the protocol by an individual participant will require an office visit of approximately one hour followed by an overnight laboratory visit of approximately 12 hours, to take place within a six week period. If convenient, the two visits may be combined. Total enrollment duration for an individual participant will not exceed six weeks; it is estimated that the entire study duration will not exceed nine months.

5.2. Scientific Rationale for Study Design

The study has been designed to align with the Standards for Reporting Diagnostic Accuracy (STARD) statement.[8]

5.3. Justification of Treatment Regimen and Duration

No treatment will be implemented during this study.

5.4. Measures to Minimize Bias

This study is designed for the purpose of diagnostic validation, and therefore randomization and blinding will not take place.

5.5. End of Study Definition

The study will be considered complete when participants are no longer being examined or the last participant's last study visit has occurred.

A participant is considered to have completed the study if he or she has completed all phases of the study including the last visit or the last scheduled procedure shown in the Schedule of Activities.

6. STUDY PARTICIPANTS

The COVID-19 pandemic is an ongoing and evolving situation. Each site will implement screening procedures that align with their local state and federal guidelines. These procedures are not listed as formal entry criteria.

6.1. Inclusion Criteria

Subjects must meet all of the following inclusion criteria:

- INCL1: Aged ≥18 years;
- INCL2: Fluent in English;
- INCL 3: Able to provide informed consent.

6.2. Exclusion Criteria

Subjects shall be excluded if any of the following are present:

- EXCL 1: Self-reported habitual sleep duration of <4 hours/night on average ("How many hours sleep do you usually get per night?");
- EXCL 2: Circadian phase disorder, shift work, or any other issue/condition that would, in the opinion of the site investigator, reduce the likelihood of obtaining at least four hours of sleep during the overnight study;
- EXCL 3: History of allergic reactions to medical adhesives;
- EXCL 4: Skin rash or other dermatological condition that would impact correct placement of the DreamKit device and/or PSG sensors, and/or would be exacerbated by the presence of the device or sensors;
- EXCL 5: Presence of a pacemaker;
- EXCL 6: Severe medical condition (controlled or uncontrolled) that would impede data collection in the opinion of the site investigator, including the requirement for oxygen therapy;
- EXCL 7 [for those currently using overnight therapy]: Unwilling to withdraw from overnight therapy for a single night and/or clinically unsuitable to withdraw from overnight therapy in the opinion of the site investigator, with overnight therapy including but not limited to any form of PAP or ventilation, oral device including mandibular advancement devices or mouthguard for bruxism, nasal dilator strips, and/or positional device;

- EXCL 8 [for those currently using overnight therapy]: Considered by the site investigator to be at risk of an AE resulting from hypersomnolence the day after the overnight visit, such as a high-risk occupation including but not limited to a pilot or commercial driver;
- EXCL 9: An employee, or family member of an employee, of a company that designs, sells, or manufactures sleep related products (including Philips).

6.3. Enrollment

All participants who sign the consent form will be considered enrolled, even if they do not complete the study.

6.4. Screen Failures

Participants who consent to participate in the study, but who do not meet one or more criteria required for participation, will be considered screen failures. Minimal information will be collected for such participants, including demographics, screen failure details, eligibility criteria, and any AEs.

Re-screening is possible if, in the opinion of the Principal Investigator or their designee, the reason for the original screen fail is likely to have changed and will not impact participant safety or data integrity. Re-screened participants should be assigned the same participant number as used for the initial screening.

6.5. Strategies for Recruitment and Retention

Participants will be recruited such that the overall sample will comprise approximately 50% OSA, 30% central sleep apnea (CSA; with or without Cheyne-Stokes respiration), and 20% healthy (no SDB). Recruitment for the OSA and CSA participants will proceed by targeting those with a known diagnosis and/or those currently using therapy for SDB and/or those considered by the site investigator to be high-risk. The sites may choose to administer the STOP-BANG questionnaire[9] during phone screening for risk stratification, but this is optional. Due to night-to-night SDB severity variability as well as the natural history of SDB, the diagnosis of each participant may not be known ahead of time and as such, our inclusion/exclusion criteria do not reference OSA or CSA diagnostic criteria.

The PSGs will be scored throughout the study, and each participant will be assigned to a diagnostic category (see Section 8.1.6). This information will be used to guide further recruitment to ensure the proportions of OSA, CSA, and no SDB referenced above, as well as to ensure a wide range of SDB severity. The diagnostic category assigned in this study will be based solely on PSG scoring output without any other clinical information, and will have no bearing on clinical care.

It is anticipated that racial/ethnic minorities will represent at least 20% of the sample, and that males and females will comprise at least 30% of the sample each. These parameters are approximate expectations only.

All participants will be enrolled within the US. Recruitment will be the responsibility of the site, and will take place through advertisements, the pipeline at local clinic/s, and/or by inspection of local medical records. As this study has only two visits, it is not likely that participants will drop-out or be lost to follow-up before study completion and therefore no specific strategies for retention are required.

7. STUDY INTERVENTION

The DreamKit device is a non-released, investigational product. The previous generation device, SomnaPatch, is FDA-approved (K183625); however, the DreamKit device has been modified from this version.

The actigraphy device (GENEActiv Original; Activinsights, United Kingdom) is a released, 510(k) exempt product. PSGs will be acquired through a variety of platforms; all are released products. Released products will be utilized according to their intended use.

7.1. Acquisition and Accountability

All devices (used and un-used) will be shipped to the sites and then returned to the Sponsor at the end of the study. An inventory of devices will be maintained.

7.2. Formulation, Appearance, Packaging, and Labeling

The DreamKit Device Label, User Manual and Operating Manual are included with the IRB submission. Some content of these documents may change before regulatory submission.

7.3. Product Storage and Stability

The DreamKit device should not be used in temperatures above 35 degrees Celsius (95 degrees Fahrenheit).

7.4. Preparation

The DreamKit devices are single use, and do not require configuration prior to use. The investigator is required to peel off the adhesive backing, and place the forehead patch above the eyebrows in the center of the forehead, after thoroughly prepping the skin. Calibration of the device begins automatically without user input, taking approximately five minutes to complete.

8. STUDY PROCEDURES & EVALUATIONS

8.1. Efficacy Assessments

8.1.1. Phone screening

Recruitment will be the responsibility of the sites. Potential participants will be screened over the phone for eligibility, and then scheduled for an enrollment visit. The sites may choose to administer the STOP-BANG questionnaire during phone screening for SDB risk stratification, but this is optional and responses will not be captured in the dataset.

8.1.2. Visit 1: Office visit for enrollment

Preliminary assessment of eligibility will be performed by the site investigator or their designee during Visit 1, which is anticipated to take approximately one hour. The investigator or their designee will then describe the purpose of the study, all study procedures, and possible risks of participation. After an opportunity to ask questions, consent will be sought by the investigator or their designee.

Following consent, an investigator will perform a brief physical examination and medical history, including anthropometric measurements (height; weight; neck, waist, and hip circumferences). The examination will include vital signs (blood pressure obtained while seated according to American Heart Association guidelines,[10] pulse rate, respiratory rate, and SpO_2).

Participants will then complete a brief battery of questionnaires including a descriptive questionnaire (including sociodemographics, usual sleep routine, and current medical conditions); the Epworth Sleepiness Scale;[11] the Fitzpatrick skin type questionnaire;[12] and the short-form versions of the Patient-Reported Outcomes Measurement Information Systems (PROMIS) sleep disturbance and sleep-related impairment surveys.[13]

If the participant is found to be eligible, they will be scheduled for Visit 2 within six weeks of the enrollment visit. Note that the office visit (enrollment) and the laboratory visit (testing) may be combined, if logistically feasible.

8.1.3. Visit 2: Overnight laboratory visit for testing

Participants will be asked to attend Visit 2 for overnight testing. The visit is anticipated to take approximately 12 hours. Prior to any testing, each participant will be guided through what to expect during the visit.

Polysomnography

A registered polysomnographic technologist (RPSGT) or otherwise qualified individual will be responsible for setting up and overseeing the PSG according to AASM guidelines. The PSG will include, at minimum,

electroencephalography (EEG; F4-M1, C4-M1, O2-M1, with back-up signals F3-M2, C3-M2, O1-M2), electrooculography (EOG; E1-M2 and E2-M2), electrocardiography (ECG), chin electromyography (EMG; ChinZ, Chin1, and Chin2), leg EMG (longitudinally and symmetrically over the middle of each anterior tibialis), pulse oximetry, airflow assessed by nasal pressure and oronasal thermistry, thoracic and abdominal respiratory inductance plethysmography (RIP) belts, and body position (supine, lateral, prone). The PSG will include a digital video recording per AASM recommendations.[14] Electrode placement specifications are from the AASM scoring rules Section IV Part 1.

Placement of DreamKit device

A DreamKit device will be placed on each participant per the supplied instructions. Thorough skin preparation is required before placement. As the PSG and HSAT both require nasal cannulae, Philips will supply a 't-tube' allowing a single nasal cannula to contribute an airflow signal to both platforms.

Placement of actigraphy device

The participant ID, sampling frequency (20Hz) and measurement duration (set to 7 days) are required in order to configure each actigraphy device using the GENEActiv software that will be supplied to study sites. Following configuration, the actigraphy device will be placed on the non-dominant wrist, and recording initiated. A bandage/gauze can be placed underneath the device if desired. The actigraphy device will stay in place until the completion of the PSG. The GENEActiv configuration/download software should be installed on the same computer that runs the PSG platform, to ensure synchronization by using the same timestamp.

Note that if a participant is unwilling or unable to wear the actigraphy device, for example due to a dermatological condition, they can complete the remainder of the protocol without actigraphy.

PSG calibration procedure

After initiating the recording but prior to lights-out, the RPSGT will work through the following calibration/bio-calibration procedure:

- Perform and document an impedance check of the EEG, EOG, and EMG electrodes;
- Record a minimum of 30 seconds of EEG with participant awake lying quietly with eyes open;
- Record a minimum of 30 seconds of EEG with participant awake lying quietly with closed open;
- Ask the participant to look up and down without moving head (x5);
- Ask the participant to look left and right without moving head (x5);
- Ask the participant to blink (x5);
- Ask the participant to grit teeth and /or chew (5 seconds);

- Ask the participant to simulate a snore or hum (5 seconds);
- Ask the participant to breathe normally and ensure that airflow and respiratory effort signals are synchronized;
- Ask the participant to perform a breath-hold (10 seconds);
- Ask the participant to breathe normally and upon instruction, take a breath in and out, while checking polarity and mark the in/out accordingly;
- Ask the participant to breathe through the nose only (10 seconds);
- Ask the participant to breathe through the mouth only (10 seconds);
- Ask the participant to take a deep breath and hold it, and while holding his/her breath push the stomach in and out 4 times;
- Ask the participant to flex the left foot/raise toes on left foot (x5);
- Ask the participant to flex the left foot/raise toes on right foot (x5).

Overnight monitoring

The technologist responsible for the PSG will ensure that all signals are free from artifact at study initiation. If sensors become dislodged, the technologist will endeavor to reattach or replace in order to obtain high-quality signals throughout the night. The technologist will complete a case report form (CRF) logging the exact lights off and lights on times, as well as any signal quality or other issues that arise during each PSG.

Morning procedure

In the morning, the technologist will remove all sensors and the participant will be free to leave the laboratory.

Data transfer and device returns

Study staff will download the raw PSG, DreamKit, and actigraphy data files using the appropriate software provided, and send all electronic data files to Philips using an approved, encrypted method. Alternatively, the DreamKit devices will be returned allowing the data download to take place at Philips. The adhesive backing will be replaced on each DreamKit device before returning the devices to Philips. The actigraphy devices will be cleaned and re-used, and returned to Philips at the end of the study.

8.1.4. Adverse event monitoring

AE monitoring will take place throughout the study. Participants will be provided with contact details should any AEs arise following the final study visit.

8.1.5. Data processing and scoring

All data processing will take place at Philips using Sleepware software. The analyst will import the DreamKit and PSG signals, ensuring that the signals are mapped correctly. The analyst will then inspect the time alignment of the DreamKit and PSG signals; if necessary, the DreamKit time may be adjusted to ensure synchronization with the PSG pulse rate and/or flow signal/s recorded from the shared nasal cannula.

Automated scoring using Somnolyzer will be used for PSG and DreamKit respiratory event detection within the rest period (time between lights off and lights on). Sleep staging during the rest period will be undertaken using Somnolyzer (PSG) or CReSS (DreamKit) algorithms. Sleep staging and event scoring will follow AASM guidelines.[14] Apneas will be scored when there is a ≥90% reduction in airflow for at least ten seconds (Section IX Part 1, G1), and classified as obstructive (continued or increased respiratory effort throughout), central (absence of respiratory effort throughout), or mixed (initial absence followed by resumption of respiratory effort). For our primary and secondary analyses, hypopneas will be scored according to the AASM recommended criteria; that is, a ≥30% reduction in airflow for at least ten seconds, associated with a SpO_2 desaturation of ≥3% (Section IX Part 1, H1A). We will perform a sensitivity analysis in which hypopneas are scored according to the alternative criteria (a ≥30% reduction in airflow for at least ten seconds, associated with a SpO_2 desaturation of ≥4%; Section IX Part 1, H1B).

The following metrics will be calculated for both the PSG and DreamKit:

- AHI: Number of apneas and hypopneas divided by TST;
- CAI: Number of central apneas divided by TST;
- ODI: Number of SpO_2 desaturations (≥3%) divided by TST.

8.1.6. Signal quality and other feedback to sites

Data processing and scoring will take place throughout the study, allowing continual feedback from Philips to the sites.

The AASM clinical practice guidelines state that a diagnosis can be made using a HSAT only if the recording includes at least four hours of technically adequate oximetry and flow data;[15] studies that do not meet these criteria will not be included in the evaluable dataset. Collection of persistent invalid PSGs or other quality issues may prompt Philips to request the site to undergo troubleshooting or re-training. Note that if a PSG is excluded from the evaluable dataset for technical reasons but the investigator considers the participant to be suitable for a repeat test, a repeat overnight visit can be scheduled.

Each PSG will be categorized as follows (note that these categories are not mutually exclusive; as such, groups will be filled in the order listed below):

- PSG-CAI ≥30 events/hour (~10% of sample);

- PSG-OAI ≥30 events/hour (~17% of sample);
- PSG-CAI 15-29.9 events/hour (~10% of sample);
- PSG-OAI 15-29.9 events/hour (~17% of sample);
- PSG-CAI 5-14.9 events/hour (~10% of sample);
- PSG-OAI 5-14.9 events/hour (~17% of sample);
- PSG-AHI <5 events/hour (~20% of sample).

The proportion of participants falling into these categories across all sites will be conveyed to sites periodically, along with guidance to optimize recruitment according to the approximate goals listed in Section 6.5. Note that the category assigned during this process may differ from a clinical diagnosis; this process will take place only to ensure that recruitment proceeds according to the description in Section 6.5.

8.1.7. Compensation

Participants will be compensated $50 for the office visit and $150 for the data collection visit ($200 in total). Participants who opt to discontinue from the study will be prorated at the time of withdrawal.

8.2. Safety Assessments

All study procedures will take place during study visits, under the supervision of the Principal Investigator. The Principal Investigator is a physician and all visits will take place at a clinical facility, allowing for clinical intervention if needed. The risks associated with the study are immediate; that is, it is considered highly unlikely that an AE will take place after the completion of a study visit.

If any participants discontinue or withdraw early, for any reason including AEs, the reason will be captured.

9. DISCONTINUATION/WITHDRAWAL FROM THE STUDY

9.1. Discontinuations and Withdrawals

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Pregnancy;
- Significant study non-compliance;
- If any 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;
- Any disease progression or medical condition which requires discontinuation;
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation;
- At the discretion of the site investigator for any reason.
- If a participant wishes to voluntarily discontinue from the study, they should contact the site directly. AE monitoring will continue for all participants who voluntarily discontinue the study or are withdrawn from the study by investigators.

9.2. Lost to Follow-Up

A participant will be considered lost to follow-up if he or she fails to return for Visit 2 and is unable to be contacted by the study site staff.

9.3. Impact on Recruitment

Participants who do not complete the study will be replaced. Recruitment will continue until the evaluable dataset is complete.

10. RISK/BENEFIT ASSESSMENT

10.1. Known potential risks

A. The only anticipated adverse event (AE) related to the DreamKit device is skin irritation associated with the adhesive patch.

B. Anticipated AEs associated with PSG include skin irritation or discomfort from the sensor placement, and possible sleep fragmentation leading to hypersomnolence the following day.

C. A subset of participants may be required to withdraw from their usual overnight therapy (including but not limited to PAP, adaptive servo-ventilation, or oral appliance) during the overnight visit. Withdrawal of therapy for a single night may cause hypersomnolence the following day.

D. The PSG will include video monitoring, which may cause some discomfort to participants.

E. Some participants may feel uncomfortable answering questions regarding their sleep habits.

F. Wrist actigraphy is included as an exploratory component of the protocol (see Section 4.6). The only anticipated AE related to the actigraphy device is skin irritation associated with the placement of the device on the wrist.

10.2. Known potential benefits

Participation in this trial will not result in direct benefit to the participant.

10.3. Assessment of Potential Risks and Benefits

A. Participants reporting a history of allergic reactions to medical adhesives will not be recruited.

B. Participants reporting a history of skin rashes or atopic dermatitis will not be recruited if the condition is likely to impact the placement of, or be exacerbated by, the DreamKit and/or PSG sensors.

C. Participants who are required to be withdrawn from overnight therapy will not be recruited if they are engaged in a high-risk occupation such as commercial driving. The investigator at each site will undertake a risk assessment when considering the withdrawal of therapy for a single night, where applicable.

D. Participants will be informed about the overnight video monitoring during the consent process, and will have the option to opt-out of this component of the PSG.

E. Participants will be informed that they may choose not to answer questions that make them uncomfortable; however, this may impact their ability to participate in the remainder of the study. At minimum, completion of sociodemographic data (age, sex, race/ethnicity) is required in order to remain enrolled.

F. Participants reporting a history of skin rashes or atopic dermatitis likely to impact the placement of, or be exacerbated by, the presence of a wrist actigraphy device can complete the protocol without actigraphy. A dermatological condition impacting only the actigraphy device is not grounds for exclusion from the protocol.

It is the opinion of the Sponsor and the Principal Investigator that the benefits of this protocol outweigh the risks.

11. SAFETY MONITORING

11.1. Adverse Events and Serious Adverse Events

11.1.1. Definition of Adverse Events

An AE is any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)). When an AE is deemed to be related to the study device, it is termed an adverse device event.

11.1.2. Definition of Serious Adverse Events

An AE or suspected adverse reaction is considered serious if, in the view of either the investigator or Sponsor, it results in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. When a serious AE is deemed to be related to the study device, it is termed a serious adverse device event (SADE).

11.2. Unanticipated Adverse Device Event

An unanticipated adverse device event (UADE) is defined in 21 CFR Part 812.3(s) as “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects”.

Other important medical events which may not result in any of the outcomes above, but which may require intervention to prevent one of the outcomes above, may in the opinion of the investigator, be considered a UADE.

11.3. Classification of an Adverse Event or Adverse Device Event

11.3.1. Severity of Event

All AEs will be assessed by the study clinician using a protocol defined grading system as follows:

- Mild – Events require minimal or no treatment and do not interfere with the participant’s daily activities.

- Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

11.3.2. Relationship to the Study or Device

All AEs will have their relationship to study procedures and the study device assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- Definitely Related – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- Probably Related – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.
- Potentially Related – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- Unlikely to be related – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- Not Related – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician).

11.3.3. Expectedness

The Principal Investigator will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

11.4. Adverse Event Assessment and Follow-Up

Within 1-7 days of completing Visit 2, a phone call will allow for the assessment of any possible AEs that may have become apparent in the intervening period. Events will be followed for outcome information until resolution or stabilization

All AEs including local and systemic reactions not meeting the criteria for a serious adverse event (SAE) will be captured on the appropriate (e)CRF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

11.5. Serious Adverse Event or Serious Adverse Device Event Reporting

The study investigator shall complete a SAE or UADE Form and submit to the Sponsor and to the reviewing IRB as soon as possible, but in no event later than 24 hours (for a SAE) or 10 working days (for a UADE) after the investigator first learns of the effect. The Sponsor is responsible for conducting an evaluation of the SAE/UADE and shall report the results of such evaluation to the Food and Drug Administration (FDA) and to all reviewing IRBs and participating investigators within 24 hours (for a SAE) or 10 working days (for a UADE) after the Sponsor first receives notice of the effect. Thereafter, the Sponsor shall submit such additional reports concerning the effect as FDA requests.

11.6. Device Deficiency

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

11.7. Unanticipated Problems

11.7.1. Definition of Unanticipated Problems

An unanticipated problem (UP) is any incident, experience, or outcome that for which the nature, severity, or frequency is unexpected for the subject population or research activities as described in the current IRB approved protocol, supporting documents, and the consent form.

11.7.2. Unanticipated Problem Reporting

The Principal Investigator will submit to the Sponsor and to the reviewing IRB a report of any UADE occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect (21 CFR 812.150(a)(1)). Under 812.46(b), the Sponsor shall report the results of such evaluation to the FDA and to all reviewing IRB's and participating investigators within 10 working days after the Sponsor first receives notice of the effect. Thereafter the Sponsor shall submit such additional reports concerning the effect as FDA requests (21 CFR 812.150(b)(1)).

12. STATISTICAL CONSIDERATIONS

The statistical analysis plan has been incorporated into this protocol. It is not a stand-alone document.

12.1. Statistical Analyses

12.1.1. Sample Size Determination

The endpoint associated with Hypothesis 2 (ICC between PSG-CAI and DreamKit-CAI) exhibits a weaker effect size than the endpoint associated with Hypothesis 1 (ICC between PSG-AHI and DreamKit-AHI).

Pilot data from a sample of 178 records exhibited an ICC between the PSG-CAI and DreamKit-CAI 0.720 (95% CI 0.641 – 0.784). We will compare the lower-bound of the CI (0.641) to a threshold of 0.50, per Hypothesis 2. Assuming 90% power and an alpha of 0.05, n=195 participants will be required to test Hypothesis 2.

The same sample exhibited an ICC between the PSG-AHI and DreamKit-AHI of 0.908 (95% CI 0.879 – 0.931). We will compare the lower-bound of the CI (0.879) to a threshold of 0.75, per Hypothesis 1. Assuming 90% power and an alpha of 0.05, n=56 participants will be required to test Hypothesis 1. Thus, the sample size required for Hypothesis 2 (n=195) is more than adequate for Hypothesis 1, and we will adopt an overall sample size of n=200.

12.1.2. General Considerations

The primary and secondary analyses will be performed after excluding studies that do not meet the AASM criteria for technical adequacy described in Section 8.1.6 (evaluable dataset). Continuous data will be presented by mean, standard deviation, median, minimum, and maximum observation. Data will be presented in the untransformed and transformed format (if applicable) for each continuous variable. Categorical data will be presented as frequencies and percentages. Significance tests will be conducted at a two-sided significance level of alpha of 0.05.

12.1.3. 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.

12.1.4. Demographics and Baseline Characteristics

Participant demographics (age, sex, race/ethnicity) and descriptive characteristics will be summarized for all participants enrolled and for evaluable participants.

12.1.5. Analysis of the Primary Endpoint

We will calculate the ICC for absolute agreement (two-way, mixed effect) between the AHI-PSG and DreamKit-AHI, along with a 95% CI. Hypothesis 1 will be supported if the lower-bound of the 95% CI is equal to or above 0.75.

12.1.6. Analysis of the Secondary Endpoint

We will calculate the ICC for absolute agreement (two-way, mixed effect) between the AHI-CAI and DreamKit-CAI, along with a 95% CI. Hypothesis 2 will be supported if the lower-bound of the 95% CI is equal to or above 0.50.

For the primary and secondary endpoints, the AASM recommended definition of hypopnea will be used.

12.1.7. Adjustment for Multiplicity

We have adopted a single primary endpoint, and will progress to the secondary endpoint only if the primary hypothesis is supported. There is therefore no requirement for an adjustment to control the false discovery rate.

12.1.8. Exploratory Analyses

Analyses of indices

- We will calculate the ICC for absolute agreement (two-way, mixed effect) between the PSG and DreamKit ODI3%, total respiratory events, total apneas, total hypopneas, total obstructive apneas, total central apneas, and total mixed apneas, along with 95% CIs.
- We will construct a confusion matrix and calculate Cohen's kappa (linear weighted) for four categories of disease severity determined by the PSG and DreamKit (AHI 0-4.9, 5-14.9, 15-29.9, and ≥30 events/hour).
- We will construct a confusion matrix depicting true-positives, false-positives, true-negatives, and false-negatives for the AHI, CAI, and ODI3% (separately) at thresholds of 5, 15, 20, 30, and 40 events/hour.
- We will calculate the accuracy (percentage agreement between PSG and DreamKit), sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio for each threshold of the above indices.
- We will construct a receiver operating characteristic curve and calculate the area under the curve for each threshold of the above indices.
- We will construct a Bland-Altman plot for each threshold of the above indices, including a 95% CI for the upper and lower limits of agreement.

- We will construct a scatter plot with regression line for each threshold of the above indices.
- We will repeat all analyses listed above using the AASM alternative hypopnea criteria.

Event-level analyses

- We will construct a 2x2 confusion matrix based on the presence/absence of events by adapting the methodology described in the AASM Inter-Scorer Reliability Program: Respiratory Events (2014).[16] Each epoch staged as sleep per the PSG will be deemed 'positive' if it contains at least one respiratory event of any type, and 'negative' if it contains no respiratory event/s.
- We will construct a 4x4 confusion matrix based on apnea differentiation (obstructive apnea, central apnea, mixed apnea, no event), following the above methodology using events staged as sleep per the PSG, and calculate Cohen's kappa.[17] In cases where a single epoch contains more than one event, the first event will be used for categorization. Mixed events will be categorized independently if we observe at least five mixed events/hour in at least 5% of participants and at least ten mixed events/hour in at least 2% of participants in the evaluable dataset; otherwise, mixed events will be placed in the obstructive category to create a 3x3 confusion matrix.

Signal quality analyses

- Finally, we will compare the average percentage of useable signal quality from the DreamKit respiratory effort signal (PARE algorithm) and PSG (thoracic and/or abdominal belts).

12.2. Exploratory Analyses of Actigraphy Data

Actigraphy is included in the protocol for exploratory product development purposes only. All analyses of the actigraphy data will be conducted separately from the DreamKit analyses described above.

12.3. Safety Analyses

Safety evaluations will be performed by recording clinical AEs at the time originally reported, and they will be followed at regular intervals until resolution. AEs will be provided in data listings.

12.4. Planned Interim Analyses

No interim statistical analyses will be undertaken. There are no statistical criteria for terminating the study.

12.5. Missing Unused and Spurious Data

Imputation methods will not be employed in this study.

12.6. Deviations from the Statistical Analysis Plan

Any deviations from the original statistical plan will be noted in the analysis report.

13. OPERATIONAL CONSIDERATIONS

13.1. Regulatory and Ethical Considerations

13.1.1. Informed Consent Process

Participants will be asked to complete the consent form prior to any study procedures, including screening for eligibility.

In obtaining and documenting informed consent, the investigator must comply with applicable regulatory requirements (e.g., 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and should adhere to ICH GCP. Prior to the beginning of the trial, the investigator should have the IRB's written approval for the protocol and the written informed consent form(s) and any other written information to be provided to the participants.

Study participation is voluntary. Potential subjects, and/or their legal representatives, will be given the most current IRB-approved consent form to read. They shall be provided ample time for review and an opportunity to ask questions about the study. If they agree to participate, they shall sign the consent form and be given a copy of the signed document for their records. Each of these actions/steps will be documented. Only after informed consent has been obtained, may the remaining study procedures begin.

13.1.2. 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. 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. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to review the written consent form carefully and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. 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.

13.1.3. Study Discontinuation and Closure

Although there are no pre-determined criteria for study closure, the study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. If the study is prematurely terminated or

suspended, the Principal Investigator will promptly inform study participants, the IRB, and Sponsor, and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

- Circumstances that may warrant termination or suspension include, but are not limited to:
- Determination of unexpected, significant, or unacceptable risk to participants;
- Insufficient compliance to protocol requirements;
- Data that are not sufficiently complete and/or evaluable.

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

13.1.4. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the Sponsor. 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 without prior written approval of the Sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the Sponsor, representatives of the IRB, or regulatory agencies may 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 clinical study site will permit access to such records.

Each 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 the reviewing IRB, institutional policies, or Sponsor requirements.

Study participant research data for statistical analysis and scientific reporting will be transmitted to and stored by the Sponsor. This will not include the participant's contact 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 the Sponsor research staff will be secured and password protected. At the end of the study, all study databases will be de-identified with the exception of dates, and archived at the Sponsor.

13.2. Future Use of Stored Specimens and Data

Data collected for this study will be analyzed and stored at the Sponsor, where it may be used for future research. During the conduct of the study, an individual participant can choose to withdraw consent to

have biological specimens stored for future research. However, withdrawal of consent with regard to data storage may not be possible after the study is completed.

13.3. Safety Oversight

Safety oversight is the responsibility of the Principal Investigator. It has been determined that a Safety Monitoring Committee, Data and Safety Monitoring Board, Safety Assessment Committee and/or an Independent Safety Monitor is not required for this study.

13.4. Clinical Monitoring

This study will be monitored using a risk-based monitoring approach. It will ensure that documents used to originally record subject data (source documents) are maintained, and to verify that transcribed data are accurately reflected on the study (e)CRFs. All study documentation must be made available for review by the Sponsor or its designees as well as regulatory agencies.

13.5. Quality Assurance and Quality Control

The clinical sites will perform internal quality management of study conduct, data collection, documentation and completion.

Quality control procedures will be implemented beginning with the data entry system and data quality control checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the Sponsor, and inspection by local and regulatory authorities.

13.5.1. Data Handling and Record Keeping

The site will maintain appropriate medical and research records for this trial, in compliance with ICH GCP and regulatory and institutional requirements for the protection of confidentiality of participants.

13.5.2. Data Collection and Management Responsibilities

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

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the (e)CRF derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into a 21 CFR Part 11-compliant data capture system provided by the Sponsor. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

13.6. Study Records Retention

Study documents will be retained for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the Sponsor, if applicable. It is the responsibility of the Sponsor to inform the investigator when these documents no longer need to be retained.

13.7. Protocol Deviations

Any and all deviations from the protocol shall be documented upon discovery and reported in the subject's (e)CRFs. Significant deviations shall be reported immediately to the Sponsor.

13.8. Publication and Data Sharing Policy

The results of this clinical study may be submitted for publication. The rights for publication of results from this study remain with Philips. The Investigator must request permission from Philips prior to initiating any publication. Permission must be requested and received in writing. Review and approval of any data, abstract or manuscript is required. Philips reserves the right to delay publication to review the presentation of study methodology, data collection, data analysis, interpretation of data, proprietary information or patented technology. A request for delay and the reason(s) shall be communicated by Philips to the Investigator in writing. Philips ultimately reserves the right to deny any request to publish.

13.9. Registration

Philips will be registering this clinical study on ClinicalTrials.gov.

13.10. Conflict of Interest Policy

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest (apart from that related to Philips) of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial.

14. REFERENCES

1. Rosen IM, Kirsch DB, Chervin RD, et al. Clinical Use of a Home Sleep Apnea Test: An American Academy of Sleep Medicine Position Statement. J Clin Sleep Med 2017;13(10):1205-1207.

2. Kundel V, Shah N. Impact of Portable Sleep Testing. Sleep Med Clin 2017;12(1):137-147.

3. Kim RD, Kapur VK, Redline-Bruch J, et al. An Economic Evaluation of Home Versus Laboratory-Based Diagnosis of Obstructive Sleep Apnea. Sleep 2015;38(7):1027-1037.

4. Skomro RP, Gjevre J, Reid J, et al. Outcomes of home-based diagnosis and treatment of obstructive sleep apnea. Chest 2010;138(2):257-263.

5. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016;15(2):155-163.

6. Yalamanchali S, Farajian V, Hamilton C, Pott TR, Samuelson CG, Friedman M. Diagnosis of obstructive sleep apnea by peripheral arterial tonometry: meta-analysis. JAMA Otolaryngol Head Neck Surg 2013;139(12):1343-1350.

7. Magalang UJ, Chen NH, Cistulli PA, et al. Agreement in the scoring of respiratory events and sleep among international sleep centers. Sleep 2013;36(4):591-596.

8. Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ 2015;351(h5527.

9. Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. Chest 2016;149(3):631-638.

10. Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension 2005;45(1):142-161.

11. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14(6):540-545.

12. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988;124(6):869-871.

13. Yu L, Buysse DJ, Germain A, et al. Development of short forms from the PROMIS sleep disturbance and Sleep-Related Impairment item banks. Behav Sleep Med 2011;10(1):6-24.

14. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). J Clin Sleep Med 2017;13(5):665-666.

15. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13(3):479-504.

16. Rosenberg RS, Van Hout S. The American Academy of Sleep Medicine Inter-scorer Reliability program: respiratory events. J Clin Sleep Med 2014;10(4):447-454.

17. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33(1):159-174.

15. APPENDICES

A. Informed consent form

B. DreamKit Device Label

C. DreamKit User Manual

D. DreamKit Operating Manual

E. Descriptive questionnaire

F. Epworth Sleepiness Scale

G. Fitzpatrick skin type questionnaire

H. Short-form PROMIS sleep disturbance survey

I. Short-form PROMIS sleep-related impairment survey

J. STOP-BANG questionnaire

16. INVESTIGATOR'S STATEMENT

I agree to conduct the trial as outlined in the protocol in accordance with the Sponsor's guidelines, Good Clinical Practices, the Declaration of Helsinki, and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB. The Sponsor's guidelines include, but are not limited to:

- Provide Philips with current curriculum vitae including a statement regarding relevant experience.
- Provide accurate financial disclosure information to allow Philips to make an accurate disclosure statement as required under 21 CFR, Part 54 for the course of the investigation and for up to one year after its completion
- Provide supervision of all testing of the device involving human subjects.
- If applicable, provide Philips with information regarding past investigations or other research that was terminated, including an explanation of the circumstances that led to the termination.
- Permission to allow Philips and/or regulatory agencies to inspect study facilities and pertinent records at reasonable times and in a reasonable manner that ensures subject confidentiality. If this study is to be inspected by a regulatory agency, Philips is to be notified as soon as possible.
- Submission of the proposed clinical investigation including the protocol and the consent form to an IRB for approval and the acquisition of written approval for each subject ensuring that the requirements for obtaining informed consent are obtained prior to the use of any test articles.
- Submission of any proposed change in or significant deviation from the protocol to the IRB using a signed formal amendment document prepared by the Sponsor. Any proposed changes or deviations from the protocol require that the informed consent also reflects such changes or deviations and that the revised informed consent be approved by an IRB.
- Documentation and explanation of individual protocol deviations and violations are captured with explanations as indicated.
- Submission of reports of AEs to the Sponsor and IRB as outlined in the protocol.
- Submission of timely progress reports to the IRB and Sponsor at appropriate intervals on a schedule determined by the IRB or Sponsor, as indicated.
- Record keeping: the Investigator shall maintain adequate and accurate records designed to record completion of all study procedures, related observations and other key data (such as safety, compliance and product accountability) pertinent to the investigation on each subject enrolled. The investigator must maintain these records for a period as specified by Philips following completion of the study report.

I agree that all information provided to me by the Sponsor including pre-clinical data, protocols, electronic databases, (e)CRFs, and verbal and written information shall be kept strictly confidential and confined to the clinical personnel involved in conduct of the trial. It is recognized that this information may be related in confidence to the IRB. I also understand that reports or information about the trial or its progress shall not be provided to anyone not involved in the trial other than the Sponsor or other legally constituted authority.

[redacted]

Principal Investigator Signature and Printed Name

[redacted]

Date