Title: Clinical study for the BONGO device in the treatment of obstructive sleep apnea

Funding Sponsor:	InnoMed Healthscience 6601 Lyons Road, Buildings B1 - B4 Coconut Creek, FL 33073
Study Product:	BONGO
Protocol Number:	INN-C003V1.0
Primary Investigators:	Jerrold Kram MD California Center for Sleep Disorders 985 Atlantic Ave. Suite 250 Alameda, CA 94501 (510) 263-3300

Date of Original Version V1.0: July 11, 2016

Study Acknowledgement and Signature Page

I understand that this protocol may contain information that is confidential and proprietary to InnoMed Healthscience.

I have read this protocol and agree that it contains all of the components and details necessary to conduct the study as described. I will conduct the study according to good clinical practices and any regulatory requirements deemed necessary.

This is to include supervision of staff participating in this research project, completion of the case report forms/data collection forms, obtaining Institutional Review Board (IRB) approval prior to enrolling any subject and make all attempts to conduct within the time frames allocated. I further agree to keep confidential any information gleaned from the conduct of the study and/or InnoMed Healthscience.

I have read this clinical investigational protocol and fully agree with the contents.

_____
Printed Name of Investigator

_____ _____
Investigator Signature Date Signed

Protocol Number INN-C003V1.0

Table of Contents

1 List of Abbreviations

AHI	Apnea Hypopnea Index
APAP	Auto-titrating CPAP
CFR	Code of Federal Regulation
CPAP	Continuous Positive Airway Pressure
CRF	Case Report Form(s)
CV	Clinic Visit
EPAP	Expiratory positive airway pressure
GCP	Good Clinical Practice(s)
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnea
PHI	Protected Health Information
PSG	Polysomnogram
IRB	Institutional Review Board

2 Study Summary

Title	Clinical study for the BONGO device in the treatment of obstructive sleep apnea.
Short Title	Clinical Study – BONGO Device
Protocol Number	INN-C003
Methodology	Prospective, non-randomized, open label study
Study Center(s)	1
Primary Endpoint	AHI with Bongo at PSG 2 compared to baseline study
Number of Subjects	Up to 10 subjects who complete
Diagnosis and Main Inclusion Criteria	• ≥ 21 years of age • Diagnosis of mild to moderate obstructive sleep apnea via a PSG within the last 12 months
Study Product /Indication for Use	BONGO NASAL EPAP Device Intended for adult patients for the treatment of mild to moderate obstructive sleep apnea
Control/Comparator	None

3 Introduction

This document is a protocol for a human research study. This study is to be conducted according to US (21 CFR Part 812) and international standards of Good Clinical Practice (International Conference on Harmonization ICH-E6, ISO 14155 and other applicable government regulations, and Institutional research policies and procedures).

3.1 Background

Sleep is a necessary component of good health and comprises about one-third of a human life. The average person sleeps about 3000 hours per year; thus, the importance of sleep should not be underestimated. Adequate quantity and quality of sleep is essential to most psychological and physiological processes. Obstructive sleep apnea (OSA) is a common and serious condition that impairs sleep and can compromise an individual's health.

OSA can be characterized by a periodic full closure or partial obstruction in the upper airway due to neurological and/or anatomical features factors including micro- and retrognathia and impaired neuromodulation to the upper airway. Risk factors also include obesity, male, or post-menopausal females, age, neck size, and upper airway malformations such as deviated septum (Epstein, et al., 2009; Kapur, 2010). The obstruction or upper airways resistance results in cyclical reductions in blood oxygen, increased work of breathing, and arousals (cortical and sympathetic) from sleep. These sequelae may in turn have short- or long-term results such as insulin resistance, type two diabetes, stroke, incident coronary heart disease in men, neurocognitive deficits, and hypertension. Along with damage to health, these conditions may and also have significant negative workplace and economic consequences (Gottlieb et al., 2010; Marin, et al., 2005; Redeker & McEnany, 2011; Redline et al., 2010; Rosekind, et al., 2010; Yaggi;, 2005).

Continuous positive airway pressure (CPAP) is the most often frequently prescribed therapy for OSA. CPAP provides a pneumatic splint to the upper airway, thus preventing closure due to critical closing pressure. Other therapeutic options include oral appliances, surgical procedures, and, most recently, expiratory positive airway pressure (EPAP) devices (Provent K071560; K080983; K090398; K102404, Theravent, San Jose).

While CPAP is considered the therapy of choice, adherence to short-term (acclimation) and long-term therapy remains problematic (Somers, Peterson, Sharma & Yaramchuc, 2011). Rates of adherence, defined as usage of at least 4 hours for 70 percent of the nights, are reported to average between 30% and 60%; one study found that 31% of their population did not fill their prescription for CPAP (Sin, Mayer, Man & Pawluk, 2002; Wolkove, Baltzan, Kamel, Dabrusin & Palayew, 2008). Thus there is still an opportunity to improve therapeutic targets for patients with OSA.

Expiratory positive airway pressure (EPAP) is such a therapeutic target. Data support the use of the EPAP for the treatment of OSA. At least two potential mechanisms of action have been suggested. One of these is increased functional residual capacity,

which produces tracheal traction, resulting in lessened propensity for upper airway/pharyngeal collapse. An alternative mechanism is passive dilation of the airway, which reduces flow limitation (Braga, Chen, Burschtin, Rapoport & Ayappa, 2011; Colrain, Brooks & Black, 2008; Heinzer et al., 2008; Owens et al., 2012; Rosenthal, Massie, Dolan, Loomas, Kram & Hart, 2009; Walsh et al., 2011).

The Provent device provides for an “unimpeded flow of air during inhalation, but closes so that exhalation occurs against a fixed orifice” thus creating EPAP (Rosenthal, et al, 2009). The Provent device is comprised of two nasal inserts which are affixed to the nares via adhesive, each containing an actuated valve. Several studies provide the long-term (up to 12 months) effectiveness of Provent versus sham devices in multicenter trial with up to 250 subjects enrolled. These studies demonstrated an effective therapeutic approach in reducing the apnea hypopnea values (Berry et al., 2010;Kryger, et al., 2011). These studies further demonstrated that no serious adverse events occurred over the span of the study.

The BONGO NASAL EPAP device was developed to provide similar principals of operation and is posited to be substantially equivalent to the Provent device. This mechanism provides for minimal inhale resistance and controlled exhale resistance which increases expiratory airway pressure upon exhalation as noted above.

The Bongo differs from the Provent in that it is reusable, does not use adhesive, and seals against the opening of the nares instead of the outer edges of the nares and nose. During product development, bench testing was conducted on the Bongo, including age testing, environmental testing (high temperature, low temperature, and humidity), cycle testing, drop testing, and cleaning testing. Comparative testing against the Provent device was also conducted including inhale resistance testing and exhalation flow rate testing.

3.2 Investigational Product Description

The BONGO NASAL EPAP device consists of two nasal inserts (a connected pair), each containing an actuated valve, with a patient attachment mechanism. The device works by providing an inhalation port that offers minimal inhale resistance during inhalation, but is closed by the actuated valve so that exhalation occurs against a fixed orifice. This mechanism provides increased EPAP upon exhalation.

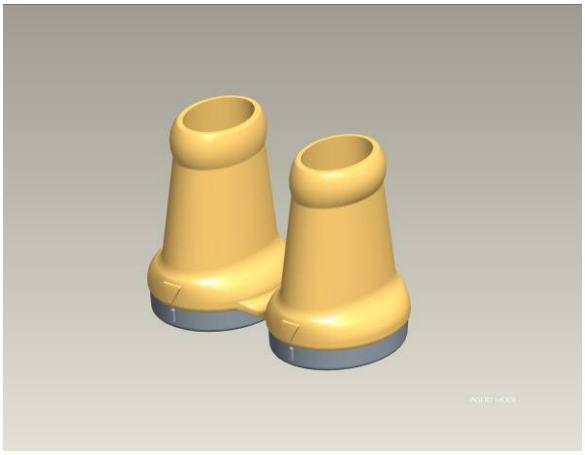
The design incorporates elements of the currently marketed Nasal-Aire II (K022465). The Nasal-Aire II is a nasal interface that delivers positive pressure from the CPAP machine to the patient. The materials to be used in the investigational product are similar to those in the currently marketed product. Like the Nasal-Aire II, the Bongo will seal against the nares.

Nasal-Aire II

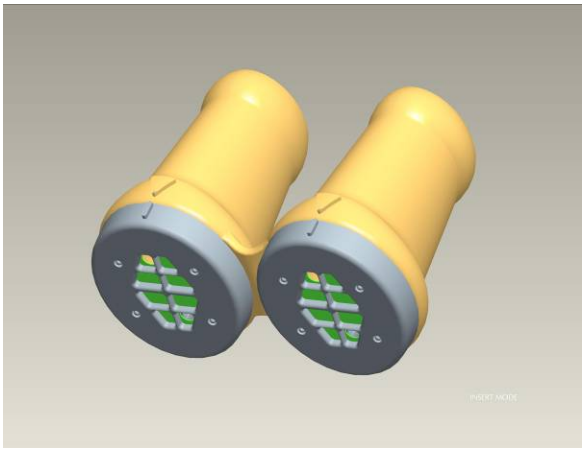
Nasal-Aire II in Use

Nasal Inserts of Nasal-Aire II

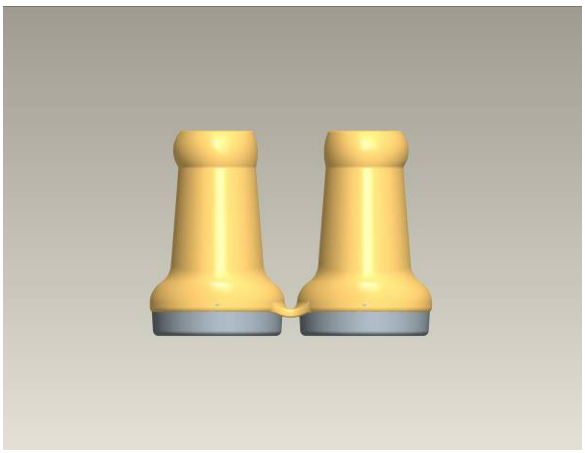
Bongo Renderings



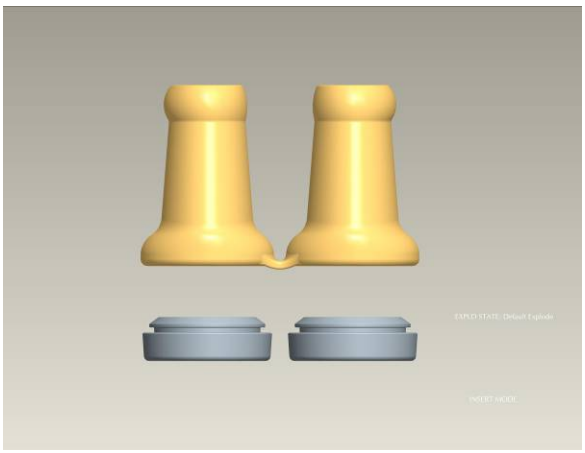
Top View



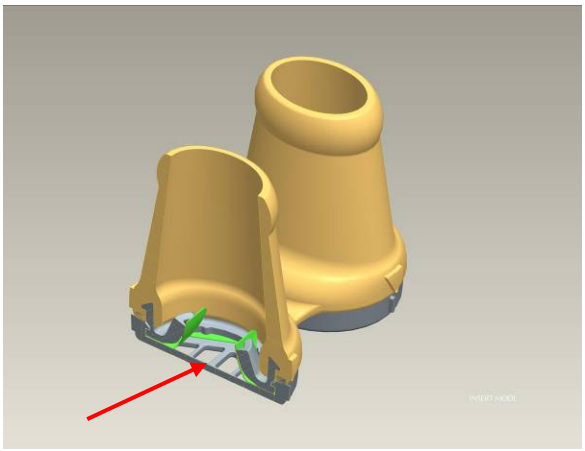
Bottom View



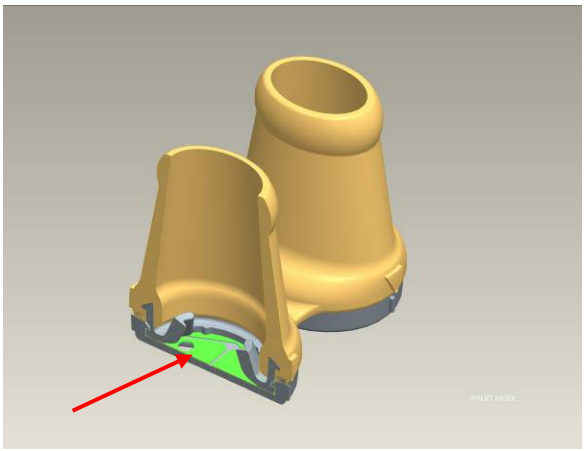
Front View



Exploded View
(Nasal Inserts in Yellow
Valves in Gray)



Cross-section showing Valve OPEN



Cross-section showing Valve CLOSED

The Bongo is made of silicone and polypropylene. A total of four (4) nasal insert sizes (SM, MD, LG, and XL) will be available during this study. Subjects will fit the most appropriate size for comfort during the first clinic visit. A total of two (2) valves with different resistances (R1 and R2) will be available during this study. Each nasal insert size will have the capability to use each resistor for a total of 8 variations (e.g. Nasal Insert MD will have R1 and R2 options).

4 Study Overview

4.1 Study Objectives

The objective for this study is to provide the data required for inclusion within a pre-market notification (510k) submission. The study design and end points have previously been discussed with the Food and Drug Administration.

4.2 Primary Endpoint

The primary endpoint for the study is change in AHI, defined as the difference in AHI between the diagnostic study and PSG 2 with the Bongo. A reduction in AHI to less than 10 or an AHI reduction by at least 50% from the baseline is considered clinically significant.

5 Study Design and Procedural Detail

5.1 Study Outline and Design

This study is a prospective, non-randomized, open label, single-center clinical study for the BONGO NASAL EPAP device for the treatment of obstructive sleep apnea.

Subjects will have the following study schedule:

1. Screening
2. In-lab PSG 1 with the Bongo
3. 2 week at home use of the Bongo
4. In-lab PSG 2 with the Bongo
5. Study termination visit (may be completed the morning following PSG 2)

5.2 Subject Recruitment and Screening

Subjects will be recruited from existing patient rolls within the participating sleep center. The patient rolls provide the first line of screening for inclusion criteria and exclusion criteria. Phone screening will be conducted to further assess meeting the inclusion criteria and exclusion criteria (e.g. do they use a full face mask or are they mouth breathers).Additional screening will be conducted during the screening visit. Data obtained from screening will not be retained and the site will follow their standard procedures for destroying the data.

5.3 Method for Assigning Subjects

Subjects will not be randomized for this study

5.4 Concomitant Therapy

Subjects will take their medications as normal

5.5 Blinding of Study

This study is open-label

6 Screening and Visits

6.1 Screening/Baseline

Subjects will be first phone screened using existing patient rolls at each individual sleep center. Subjects who meet the initial qualifications will be asked to attend an in-clinic visit (Screening Visit).

During this Screening Visit the following will occur:

- Informed Consent Process
- Subjects will be asked to bring their CPAP/APAP machines and/or their data card for downloading and review. The following data from the past 30 days will be downloaded: pressure setting, average hours of use per night, % of time used, and residual AHI. If the subject has no data on their data card over this time period, and/or the subject has been diagnosed and is unable or willing to use CPAP, this will be noted on their record.
- Subjects will fit for the nasal inserts:
    - Subjects will select the size of the BONGO according to Bongo IFU
    - Subjects will be allowed a minimum of 10 minutes of acclimation with the valve R1; ensure that subject has some “supine” time during the acclimation period.
    - Subjects will be asked on a scale of 1-10 where their tolerability level of the device resides (<5, not qualified;≥5, will qualify to move ahead).
- Once a subject is deemed eligible to participate, baseline measurements including BMI, vital signs, medications, and the above measures will be recorded.

6.2 PSG Studies

Two in-lab PSG studies will be performed while using the Bongo device. PSG 1 will be performed on a separate visit after the Screening Visit. PSG 2 will be performed after a two week (14 day) period of at home use with the Bongo.

Sites will follow the standard sleep protocol methods that include patient preparation procedures, the standard recording montage, the proper instrument calibration and bio-calibration procedures that must precede the initiation of the collection of the PSGs according to the American Academy of Sleep Medicine (AASM) Manual for Scoring Sleep and Associated Events (2007), a standard PSG montage, recording channel labels and the order to be used will be:

- left electrooculogram (E1/M2)
- rightelectrooculogram (E2/M1)
- submental electromyogram (chin1/chin2)
- submental electromyogram (chin2/chin3)
- electroencephalogram (C3/M2)
- electroencephalogram (O2/M1)
- electroencephalogram (F4/M1)
- electroencephalogram (C4/M1)
- electrocardiogram (ECG)

- thoracic inductance plethysmography (TEFFORT)
- abdominal inductance plethysmography (AEFFORT)
- nasal/oral nasal air pressure transducer (PFLOW),
- oxygen saturation (SaO2)
- left anterior tibialis electromyogram (L LEG)
- right anterior tibialis electromyogram (R LEG)

Prior to each PSG, the site will screen the subject for acute alcohol intoxication by obtaining a breath alcohol test or equivalent. If testing shows any evidence of recent alcohol use, then the subject will be sent home after being counseled to refrain from alcohol use and return to the site within one week for the PSG. Subjects will be allowed no more than two attempts to participate if they are intoxicated upon arrival to the sleep clinic.

In addition, prior to each PSG, the site will call the subject to remind them of the upcoming PSG, they will be asked if they have any current cold or nasal condition which would prevent them from attending. At the time of the PSG, the research staff will assess the subject for nasal infection, nasal congestion, or nasal allergies that may impact the ability of the subject to breathe through the nose. If observation shows any evidence of nasal infection, nasal congestion, or nasal allergies, then the subject will be sent home and asked to return to the site after the symptoms have resolved.

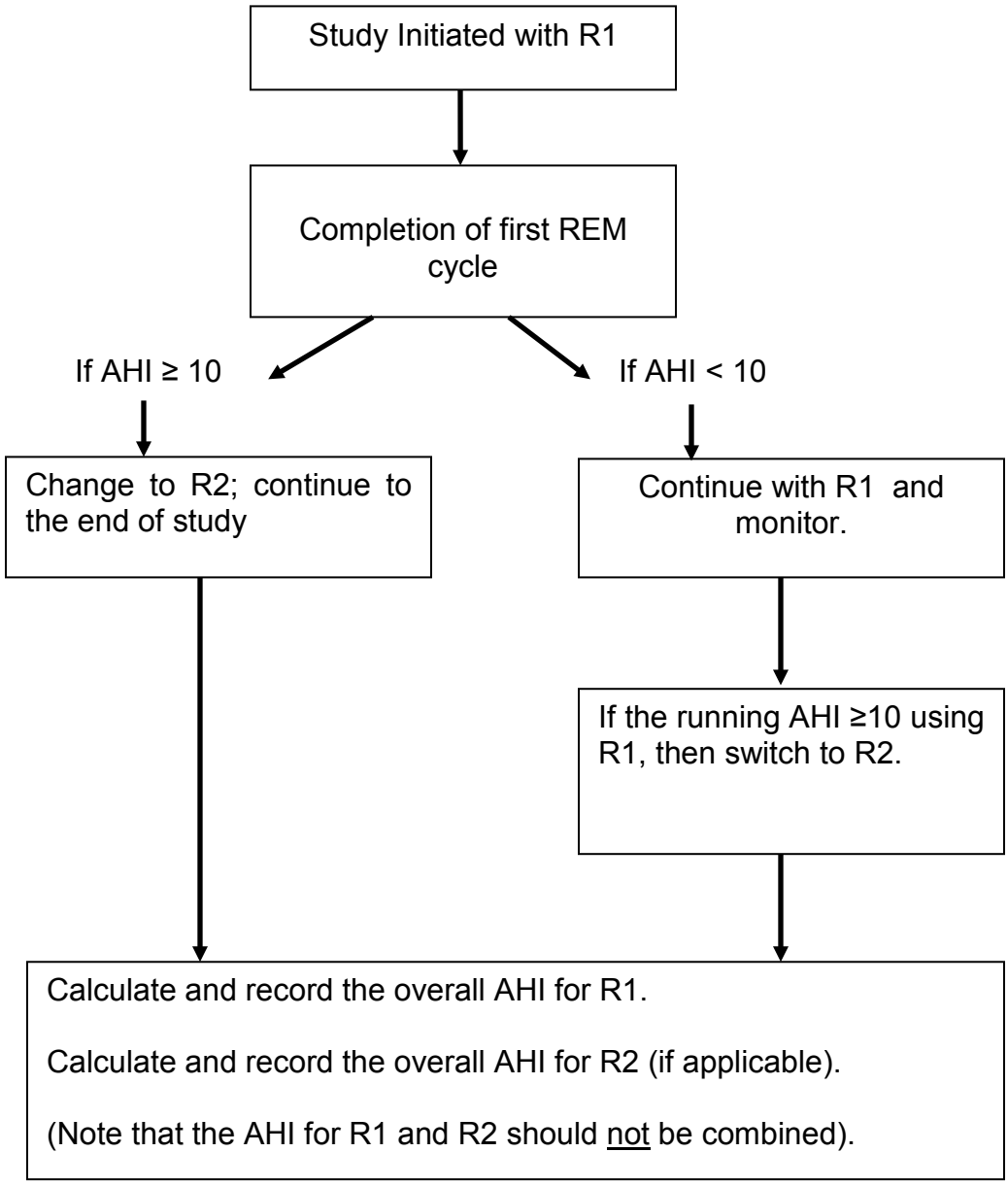
A standard type pre (PM) sleep questionnaire will also be completed at a PSG visit. This questionnaire will assess the subjects day of test activity.

To record data during a PSG with the Bongo, a sampling tube connecting the nasal insert to the pressure transducer is used. Each nasal insert has a sampling port for connecting a sampling tube. The sample tubes and instructions for use will be supplied by InnoMed to the site for this purpose.

During PSG 1:

1. Subjects may sleep in the position that is the most comfortable for them.
2. All subjects will begin with the R1 valve in place.
3. Subjects will sleep with the R1 valve until the completion of one REM cycle. Calculate the AHI at this time.
    a. If the AHI is below 10 (AHI < 10), maintain the R1 valve.
    b. If the AHI equals or exceeds 10 (AHI ≥ 10), change to the R2 valve for the remainder of PSG 1.
4. Continue to calculate the running AHI of subjects that remained on the R1.
    a. If the running AHI equals or exceeds 10 (AHI ≥ 10), change to the R2 valve for the remainder of PSG 1.

5. At the end of PSG 1 and prior to the subject leaving the facility:
    a. Calculate and record the AHI for the overall time the R1 valve was used.
    b. If applicable, also calculate and record the AHI for the overall time the R2 valve was used. (Note that the AHI for R1 and R2 should not be combined).



Prior to the subject leaving the facility, the research staff will need to score and assess whether the subject qualifies for the at home portion of the study. Score using the AASM 3% and/or arousal criteria.

1. Compare R1 AHI, as well as the R2 AHI (if applicable), to the subject's baseline AHI (from their diagnostic study).
2. If the subject while using the Bongo had an AHI reduction to less than 10 (AHI < 10) or an AHI reduction by at least 50% (AHI reduction ≥50%) compared to the baseline, then the subject qualifies for the at home portion of the study.
    a. Send the subject home with either the R1 or R2 valve only, whichever valve the subject had the lowest AHI with.
3. If the subject did not have the AHI reductions described above with either valve, then that subject will be terminated from the remainder of the study.

Subjects that qualify for the at home portion of the study will continue using the Bongo at home for two weeks. Subjects will complete a daily use log while using the Bongo at home.

Enrollment will continue until such time a total of up to 10 subjects have completed all components of the study.

In preparation for the home use portion of the study, the site will:

- Remove the sampling tubes from the Bongo and cover the Bongo sampling ports with caps provided by InnoMed prior to the subject going home
- Subjects will be provided with the instructions for use.
- Instruct the subject to call the site if any adverse events are experienced.

After two weeks (14 days) of at home use with the Bongo, the subjects will return with their Bongo unit and daily use log to the site for PSG 2. PSG 2 should be conducted no later than three days (14+3 days) after the end of the at home use portion of the study.

During PSG 2:

1. All subjects will use either the R1 or the R2 valve (the same device) that they have been using during the at home use period for the entirety of PSG 2.
2. Subjects may sleep in the position that is the most comfortable for them.
3. Calculate and record the AHI for the overall time.

Score using the AASM 3% and/or arousal criteria. PSG 2 studies to be scored no more than 3 days following the PSG 2.

6.3 Study Termination Visit

The purpose of this visit is to visually inspect the skin/nares and query the subject as to any adverse events they may have encountered and to complete the study. This visit may be conducted on the morning after the completion of their final PSG or via a separate clinic visit.

6.4 Subject Selection

As noted, subjects will be recruited from existing rolls and up to 20 subjects may be enrolled with a targeted number up to 10 subjects who complete the study.

6.5 Inclusion Criteria

- Capacity and willingness to sign informed consent
- ≥ 21 years of age
- Diagnosis of mild to moderate OSA (AHI ≥ 5 and AHI ≤ 30) within 12 months of the screening visit with the 3% hypopnea criteria
- Able to tolerate using the device during a day time trial/acclimation
- Are currently using CPAP or have been prescribed CPAP and are considered CPAP non-adherent (as per either their CPAP data card and/or verbal confirmation of a diagnosis and unwillingness to use CPAP)

6.6 Exclusion Criteria

- Nasal deformities
- Severe nasal allergies
- Rhinitis or moderate nasal congestion, acute upper respiratory (including nasal, sinus or middle ear) inflammation or infection, or perforation of the ear drum
- Co-morbid sleep disorders
- Currently on a hypnotic for insomnia (who have had insomnia for more than a month and take a hypnotic on a daily basis and/or transient insomnia being treated)
- Uncontrolled or serious illness, including but not limited to: severe breathing disorders including hypercapnic respiratory failure, respiratory muscle weakness, bullous lung disease (as seen in some types of emphysema), bypassed upper airway, pneumothorax, pneumomediastinum, etc.; severe heart disease (including heart failure); or pathologically low blood pressure.
- Full Face Mask user
- Mouth breather
- Pregnant (Female subjects of child bearing age will be asked if they are and/or planning on becoming pregnant during the study; acceptable methods of birth control include birth control pills and barrier method)

7 Task and Visit Schedule Table

	Screening Visit	PSG 1	2 week in home use	PSG 2	Term. Visit*
TASK					
Informed Consent	X				
Inclusion/Exclusion Criteria	X				
CPAP usage verification, AHI(data download)	X				
Bongo Fit	X				
Demographics	X				
Vital signs	X				
Height/Weight (BMI)	X				
Medical History	X				
Concomitant Medications	X				X
PM Questionnaire/ETOH assessment		X		X	
PSG/Scoring		X		X	
Preparation for Home Use AM Tasks		X			
CRF Completion		X		X	X
Adverse Events	X	X	X	X	X
Daily Use Diary(Subject)			X		
Daily Diary (review)					X
MD CRF review/Sign off					X

*May have this visit taking place the AM of the sleep study or in the clinic.

8 Statistical Plan

The primary aim of this study is to assess objective sleep parameters while sleeping with the BONGO NASAL EPAP device (Test product). The primary endpoint to be evaluated is AHI compared to baseline data. Baseline demographic will be summarized and reported. For continuous variables such as weight, the mean, standard deviation and range will be presented. For categorical variables such as gender, the proportion of subjects in each category will be presented. Descriptive statistics for sleep study data will be reported.

8.1 Sample Size

Up to 20 subjects may be enrolled in the study with a targeted number up to 10 subjects who complete the study and are deemed evaluable. A study with 10 subjects was proposed and accepted by the FDA for the data required for inclusion within a pre-market notification (510k) submission for the Bongo.

9 Subject Compliance Monitoring

Compliance for subject participation will be assessed at each visit.

9.1 Early Withdrawal of Subjects

Although early withdrawal of subjects is not anticipated, for subjects who withdraw prior to completion of their participation, data collected to date will be included. If the withdrawal is due to medical reasons, appropriate referral to their primary care physician will be done.

9.1.1 When and How to Withdraw Subjects

A subject may withdraw from the study at any time and for any reason. Explanation of such rights will be given to the subject during the informed consent process, both verbally and in writing. If subjects decide that they no longer wish to participate in the study, they will be asked to return for a final visit. If they are unable to comply with this request, a study termination letter will be sent to their given address. A request for the study documents will be made.

9.1.2 Data Collection and Follow-up for Withdrawn Subjects

Data will cease to be collected upon subject withdrawal of informed consent; however, data collected until the time of withdrawal will be used as appropriate and will be reported in the clinical study report.

10 Risks/Benefits

Risks

Known risks include:

- Breach of confidentiality. It is possible that information regarding subjects' clinical or laboratory evaluations will be discovered by individuals outside of study personnel, despite careful steps to protect confidentiality.
- Polysomnography: Some subjects experience mild skin irritation from electrode preparation solution, electrode adhesive, or solvents used to remove electrodes. These materials can also cause eye irritation if they come into contact with the eyes. This is a standard test for ascertaining sleep disorders in clinical practice and is widely used. Sleeping within a laboratory setting may produce psychological discomfort for some subjects.
- Subjects may feel some psychological discomfort just by the fact that they are participating in research. Such concerns include confidentiality and privacy, clinical intervention or tests adverse effects from the investigational product.

Possible Anticipated Device adverse events include:

- Headache
- Sinus Allergy
- Irritation of the nares from the nasal inserts

Benefits

Benefits include evaluation of current apnea status

11 Safety and Adverse Events

11.1 Definitions

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc…)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

Unanticipated Adverse Device Effect
An Unanticipated Adverse Device Effect is any serious adverse effect on health or safety, or any life-threatening problem or death caused by or associated with a product, 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 product that relates to the rights, safety, or welfare of subjects.

Serious injury
Any injury or illness that is any one of the following:

- life-threatening
- results in permanent impairment of a body function or permanent damage to body structure
- necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure

Adverse Event
An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse Product effect
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

11.2 Recording of Adverse Device Effects

At each contact with the subject, adverse events will be assessed. Data will be documented on an adverse event form and the subject chart. Any and all clearly study related signs, symptoms, and abnormal diagnostic procedures results should be recorded in the source document; however, events related to each other should be grouped under one diagnosis.

All adverse Product effects occurring during the study period will be recorded. The clinical course of each event will be followed until resolution or stabilization or until it has been determined that the study treatment or participation is not the cause. Serious adverse Product effects that are still ongoing at the end of the study period will be followed to determine the final outcome. Any serious adverse Product effects that occur after the study period should be recorded and reported promptly (see section 8.3 below).

11.3 Reporting of Adverse Device Effects and Unanticipated Problems

11.3.1 Investigator reporting: Notifying the study sponsor

Any events which are noted by the investigator will be reported to the sponsor not more than 10 days after learning of the event.

Sponsor contact information for reporting purposes

Report adverse Product effects by phone and facsimile to:

InnoMed Healthscience
800-200-9842 phone
877-868-8406 fax

Adverse Product Effects

Any adverse Product effect that results in serious injury or death, and any type of unanticipated adverse Product effect, regardless of seriousness or severity, must be reported to the study sponsor by telephone within 24 hours of the event.

Within the following 48 hours, the investigator shall provide further information, as applicable, on the unanticipated Product event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse Product effects shall be provided promptly to the study sponsor.

Withdrawal of IRB approval

An investigator shall report to the sponsor a withdrawal of approval by the investigator's reviewing IRB as soon as possible, but no later than 5 working days from the IRB notification of withdrawal of approval.

11.3.2 Investigator reporting: Notifying the IRB

This study will be submitted for review by a central IRB. Reporting of any reportable events will conform to IRB policy and procedures

Adverse Product Effects
All unanticipated Product effects, and all adverse Product effects resulting in research subject death or injury reported by the investigator to the study Sponsor must also be reported to the investigator's local IRB in accordance with their reporting requirements, though no later than 10 working days.

Protocol Deviations
Any protocol deviations initiated without Sponsor and/or the investigator's IRB approval that may affect the scientific soundness of the study, or affect the rights, safety, or welfare of study subjects, must be reported to the Sponsor and to the investigator's IRB as soon as a possible, but no later than 5 working days of the protocol deviation.

Reporting Process
Report unanticipated problems as defined above to the IRB using the form: as indicated on the IRB web site/portal or as a written report of the event (including a description of the event with information regarding its fulfillment of the above criteria, follow-up/resolution and need for revision to consent form and/or other study documentation).

Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's study file.

12 Receiving, Storage, Dispensing and Return

12.1 Packaging

A "fitting kit" consisting of a full set of BONGO devices with the R1 resistor will be available to study staff for sizing and acclimation purposes. These devices will be cleaned according to standard practice for cleaning CPAP masks following the facility procedures. Devices will be cleaned after each subject.

For each subject, BONGO nasal inserts of their selected size with both resistors values (R1 and R2) will be provided. If R2 is needed, the sleep technologist will replace the Bongo R1 device with the Bongo R2 device.

12.2 Receipt of Study Product

Sites will receive and log in all investigational products according to routine practices. Devices will be shipped with appropriate labeling and shipped from InnoMed.

12.3 Dispensing of Study Product

Product will be dispensed only to those subjects qualified to receive them. A device distribution log will be maintained at the site.

12.4 Return of Study Product

Used devices shall be re-inserted into their original packaging and returned to InnoMed at the completion of the study and documented on the appropriate logs.

13 Data Handling and Record Keeping

13.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Protected Health Information (PHI) collected during this study is related to general health and sleep. No additional information will be collected regarding the subject's PHI.

Review of data will be allocated to study personnel on a “need to know” basis. An enrolled subject will be assigned a unique patient ID number. Study personnel will use the patient ID number to identify all subject data on case report forms.

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

13.2 Source Documents

Source documents may include the following

- Investigator/Designee Note form
- Case report forms
- Data from the CPAP downloads
- Data from the Polysomnogram
- Self-completed questionnaires

13.3 Case Report Forms

All case report forms (CRF) will be completed in their entirety (i.e. each field filled out and or noted as not applicable). For any errors, standard good clinical practice includes the following: Each error will be crossed out with a single line, dated and initialed by the person who made the correction. Queries by the monitor will be generated for forms not completed and/or illegible

13.4 Records Retention

Records will be kept at the investigational research site for a period of no less than 2 years. Data will be kept in a secure and locked environment. It is acceptable to maintain records at an off-site facility which can be accessed within a reasonable period of time (i.e. 2 days after request).

14 Study Monitoring, Auditing, and Inspecting

14.1 Study Quality/Monitoring Plan

A study start-up meeting will be conducted to ensure all study staff are informed regarding conduct of the study and trained on the investigational product and any additional study tasks or procedures that are unique to the study. A study manual of operations (MOP) will be provided to the site to enhance GCP of the site.

It is anticipated that this study will be monitored at least once during the course of the study, most likely at the end of the study for all subjects enrolled. However, periodic monitoring may be conducted if deemed necessary.

14.2 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the IRB, the sponsor, government regulatory bodies, and compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data, etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable compliance and quality assurance offices.

15 Ethical and Regulatory Considerations

This study falls under the abbreviated requirements for a non-significant risk study (NSR, 21 CFR Part 812). As such this study will be conducted in compliance with the requirements of same. This study is to be conducted according to US regulations and international standards for Good Clinical Practice, including 21 CFR Parts 50, 54, 56 and the International Conference on Harmonization guidelines (E-6) and ISO 14155 as applicable. In addition institutional research policies and procedures deemed necessary to conduct this research.

This protocol and any amendments will be submitted to a properly constituted independent Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study. The investigator should provide the sponsor with a list of IRB members and their affiliates.

All subjects for this study will be provided a consent form describing this study and will be provided sufficient information to make an informed decision about their participation in this study. For sites located in California, the Experimental Subject's Bill of Rights will also be provided.

See the accompanying copy of the Subject Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the IRB for this study. The formal consent of a subject, using the IRB-approved consent form, will be obtained prior to that subject undergoing any study procedure. The consent form must be signed by the subject and by the investigator or designee obtaining the consent.

16 Study Finances

16.1 Funding Source

This study is being funded by InnoMed Healthscience

16.2 Conflict of Interest

In accordance with good clinical practices, the principal investigator and/or staff will provide a signed conflict of interest statement which will include any financial relationship with the sponsor.

16.3 Subject Stipends or Payments

Subjects will be given a stipend for their participation

17 Publication Plan

The data from this study may be used for publication. If publication is sought, normal precautions with regards to subject confidentiality and privacy will be maintained.

18 References

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