The Evaluation of a Nasal Mask for the Treatment of Obstructive Sleep Apnea

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DATE: 12th March 2017

Fisher & Paykel HEALTHCARE

Fisher & Paykel
HEALTHCARE

Clinical Investigation Plan

March 2017

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1.1. List of Abbreviations

AE	Adverse Event
AHI	Apnea Hypopnea Index
APAP	Automatic Positive Airway Pressure
Bi-level PAP	Bi-level Positive Airway Pressure
CIA	Clinical Investigation Administration
CIP	Clinical Investigation Plan
CPAP	Continuous Positive Airway Pressure
CRF	Case Report Form
FPH	Fisher & Paykel Healthcare
GCP	Good Clinical Practice
HA	Hazard Analysis
IB	Investigators Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IRB	Independent Review Board
NTLSC	North Texas Lung & Sleep Clinic
OSA	Obstructive Sleep Apnea
PAP	Positive Airway Pressure
SAE	Serious Adverse Event
UI	User Instructions

[redacted]

2. Document Information

2.1. Purpose and Scope

The purpose of the trial is to evaluate the performance, comfort and ease of use of the F&P Nasal Mask in the home environment.

2.2. Confidentiality Statement

This document contains confidential information belonging to Fisher & Paykel Healthcare and is provided for the sole purpose of enabling an evaluation of a possible collaboration with Fisher & Paykel Healthcare to undertake the proposed clinical research. This document must be maintained in a confidential manner at all times and any disclosure, distribution or reproduction of this document outside the intended purpose is prohibited.

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2.4. Monitoring Arrangements

FPH will be conducting the study, and as such the investigators or their nominees will monitor the progress of the investigation. The principal investigator will have access to all source documents needed to verify the entries on the Case Report Forms (CRF) and other protocol related documents; provided that participant confidentiality is maintained in agreement with local regulations. It will be the principal investigator's responsibility to inspect the CRF at regular intervals throughout the investigation, to verify the adherence to the protocol and the completeness, consistency and accuracy of the data being entered on them.

The investigator's file will contain the protocol/amendments, financial disclosure form, CRFs and data clarification and query forms, Independent Review Board (IRB) approval with correspondence, informed consent, staff curriculum vitae and authorization forms, screening and enrolment logs, and other appropriate documents/correspondence as per International Conference on Harmonization (ICH) and Good Clinical Practice (GCP) and local regulations.

2.5. Data Management

Data obtained for this investigation will be recorded in source documents and attached to the CRF for both the administration of the study and collection of participant data.

Original CRFs will be stored for 15 years by FPH. Copies of the CRF will be stored on site at Clinical trial of Florida (CTF) for 15 years.

3. Investigator Information

3.1. Primary Investigator

Name: Dr. James Krainson

[redacted]

[redacted]

Address: 12600 SW 120 Street, Suite 116 & 117, Miami, FL, 33186, USA.

Email: JKrainson@ClinicaltrialsFLA.com

Phone: 305-255-2452

Professional Position: Medical Director

3.2. Coordinating Investigator

Name: David Marquez

Address: 12600 SW 120 Street, Suite 116 & 117, Miami, FL, 33186, USA.

Email: DMarquez@clinicaltrialsFLA.com

Phone: 305-255-7452

Professional Position:

3.3.

[redacted]

3.4. Institution

Name: Clinical Trials of Florida

Address: 12600 SW 120 Street, Suite 116 & 117, Miami, FL, 33186, USA.

Email: JKrainson@ClinicaltrialsFLA.com

Phone: 305-255-2452

Country of residence: United States of America

4. Sponsor Information

4.1. Primary Sponsor Details

Name of Business: Fisher & Paykel Healthcare Limited

Address: 15 Maurice Paykel Place, East Tamaki, Auckland, New Zealand.

Name of Sponsor contact person: Hanie Yee

Phone: +64 9 574 0123 Ext 7909

Email: Hanie.Yee@fphcare.co.nz

Profession: Clinical Research Manager

4.2. Overseas Representative

Sponsor: Fisher & Paykel Healthcare Inc

Country of residence: United States

[redacted]

[redacted]

Name: Robin Randolph

Address: 173 Technology Dr. Suite 100, Irvine, CA 92618

Email: robin.randolph@fphcare.com

Phone: (800) 792-3912 Ext: 2409

Professional Position: Marketing Manager, US Homecare

5. Device Information

5.1. Identification of the Medical Device

The F&P Nasal is a Nasal masks primarily used in sleep laboratories and in home use for the treatment of OSA using CPAP devices.

[redacted]

5.2. Device Risk Analysis and Management

Positive airway pressure (PAP) therapy via a nasal or oronasal mask is standard clinical practice for patients with OSA. The risks associated with this treatment are limited to the potential for slight discomfort associated with the use of a nasal/direct nasal mask during sleep. This has been mitigated with the pre-clinical testing, as described in the IB. Reporting of adverse events or adverse device effects will be included in the [redacted]

6. Justification for a Clinical Trial

6.1. Synopsis

This clinical investigation is designed to evaluate the performance (treatment efficacy and leak), comfort (subjective feedback), stability (subjective feedback, leak) as well as the participant's overall acceptance of the Nasal mask amongst OSA participants. An important factor in this investigation will be the testing of all four seal sizes (small, medium, large and wide) as well as other changes and improvements made to the design of the mask from the previous two clinical trials (Clinical trial 5 USA- CIA-195 & Clinical Trial 6 - NZ – CIA-205).

Up to 45 OSA participants who currently use a nasal or nasal pillows CPAP mask will be recruited by Clinical Trials of Florida from their database of patients. (Phone script for recruiting in Appendix A).

This study will involve a baseline visit (Visit 1) where the patient's prescribed PAP therapy treatment settings will be gathered. An F&P ICON+ device will be issued to the participant (if required) during this visit as well as gaining their informed consent for the F&P Nasal mask (CIA-211) and the Anthropometric 3D Scanning study (CIA-107). This will be followed by the participants being fitted with the F&P Nasal mask during visit 2 as well as being asked a few questions in the form of a structured questionnaire. Their initial impressions, comments and photographs will be captured via recorded audio and video (with their consent). Visit 2 will take place 7 ± 5 days after Visit 1. The

[redacted]

[redacted]

patients will come in for a final visit to return the trial mask and documentation and provide their feedback in the form of verbal comments and a structured questionnaire. Photographs will be captured as well as audio and video recorded during this visit. Visit 3 will take place 14 ± 5 days after Visit 2.

The mask and CPAP (if from the research pool) will be returned to the Institution at the conclusion of the trial and the participant will return to their previous mask and mode of device treatment. The Institution will recruit all patients within two weeks of the beginning of the study.

This study will be conducted in accordance with ICH/GCP Guidelines. No deviation from the protocol will be implemented without the prior review and approval of the sponsor except where it may be necessary to eliminate an immediate hazard to a research participant. In such case, the deviation will be reported to the sponsor as soon as possible.

6.2. Literature Review

Obstructive Sleep Apnea (OSA) is a common sleep breathing disorder affecting up to 9% of the adult population[1] and is characterized by periodic collapse of the upper airway during sleep. The standard treatment for obstructive sleep apnea is PAP, which consists of pressurized air applied to the nose via an interface. PAP includes continuous positive airway pressure (CPAP), automatic positive airway pressure (APAP) and Bilevel positive airway pressure (Bilevel PAP). Despite the effectiveness of PAP in abolishing upper airway obstruction, acceptance of and adherence with therapy has been sub-optimal[2,3]. Reasons for the low compliance include nocturnal awakenings, incorrect therapeutic pressure and primarily discomfort due to poor mask fit. Poor mask fit can result in facial abrasion, leak causing fluctuations in therapeutic pressure and irritation of the eyes[4,5].

[redacted]

6.3. Preclinical Testing

[redacted]

6.4. Previous Clinical Experience

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6.5. Justification for Administration

Participants will remain on their prescribed PAP pressure during the duration of the trial. Baseline PAP data on the participant's usual mask will be collected for up to 2 weeks in order to evaluate leak measurements and efficacy of treatment compared to the investigational mask. Participants will not be randomised to use the F&P Nasal in-home for 14 ± 4 days.

7. Objectives of the Clinical Investigation

7.1. Hypothesis

[redacted]

7.2. Objectives

Primary Objective:

[redacted]

[redacted]

- To evaluate the performance, comfort and ease of use of the F&P Nasal mask in a home environment in regards to the participants' view on overall comfort, overall experience and satisfaction.
- To gain usability insights into mask fitting and removal from all participants enrolled in this mask study.

7.3. Population

Up to 15 participants will be recruited for the trial from Fisher & Paykel Healthcare, Auckland. These include current nasal mask users.

[redacted]

7.4.

[redacted]

7.5. Essential Requirements of the Relevant Directive

Essential requirements are not applicable since this study is being conducted in the USA only.

8. Clinical Investigation Design

8.1. Type of Investigation

This is an open-label (investigators and participants are un-blinded and informed of intended treatment device) single arm study. The intended treatment F&P Nasal mask will not be randomized – as the intention is not to compare between therapies.

8.2. Controls

The PAP device data gathered from the participants using their usual mask at baseline will act as the control for each participant, and it will be compared to the data gathered from the F&P Nasal mask.

[redacted]

[redacted]

8.3. Bias

The F&P Nasal mask is non-blinded and distinguishable. Since the trial mask is the same for the entire population, this study is not blinded.

8.4. End Points

8.4.1. Primary Outcomes

Primary Outcome:

- The F&P Nasal mask is comfortable to use for the participant as measured by the custom questionnaires and recorded during the interviews.
- The mask is easy to use, accepted by the participant and provides adequate treatment for OSA during in-home use measured via custom questionnaires, logbook/sleep diary and PAP data download.
- The acceptability of the F&P Nasal through custom questionnaires

8.4.2. Secondary Outcomes

- Seal size determination using the sizing tool
- To obtain 3D face scanning and head measurements to assist with future product development (CIA-107)

8.5. Variables

Variable	Justification
Ease of use/Acceptability	To assess the ease of using the mask in the home and overall mask acceptability
Mask Comfort	To assess the comfort (or lack of) of the mask as experienced by the participant while using it in-home.
Usability of the mask	To evaluate the usability of the Nasal mask through a custom designed ease of use usability script
General Demographics	To gather participants general demographics

[redacted]

[redacted]

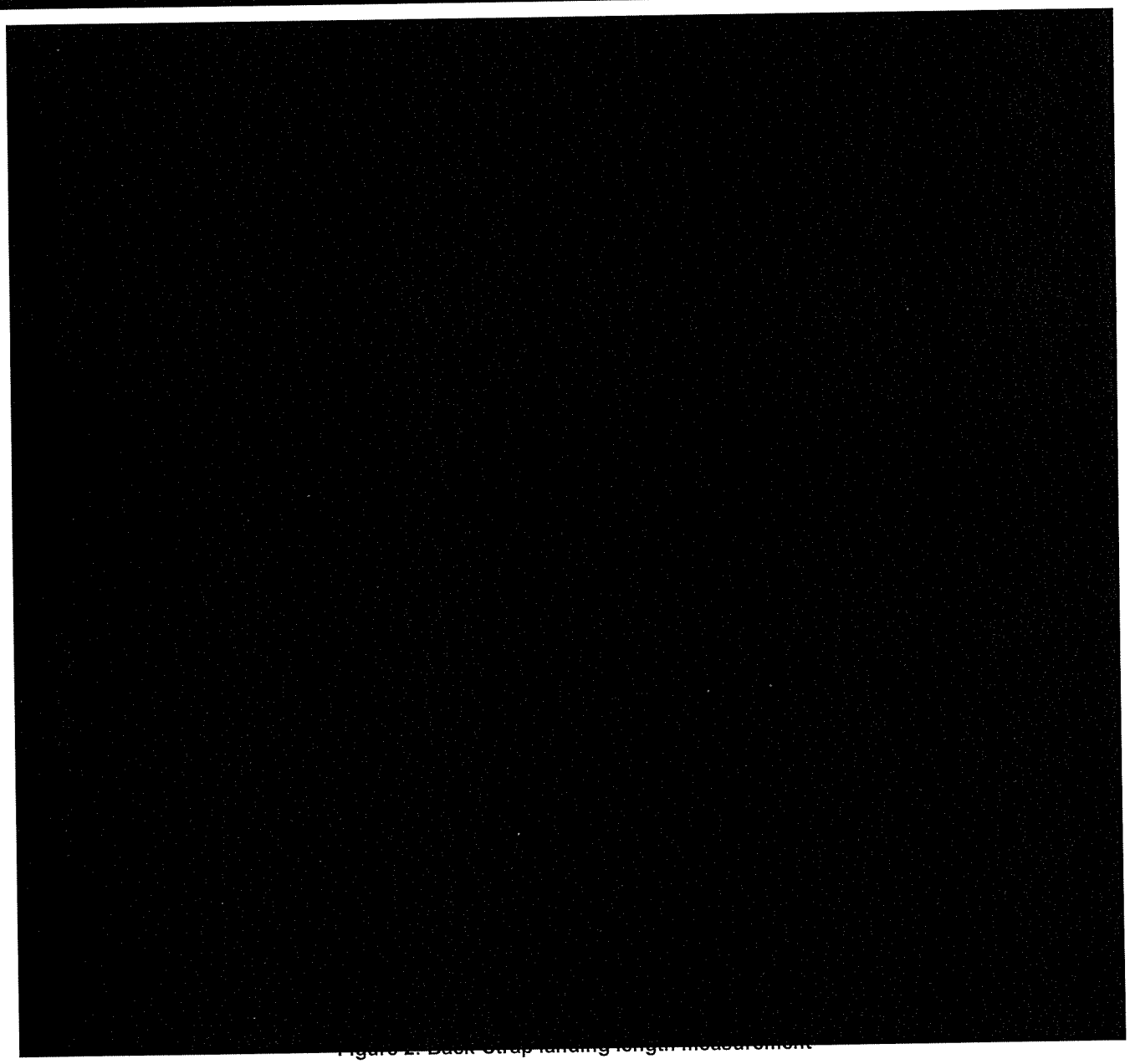
Preference	To assess which mask the participants prefers to use going forward.	[redacted]
Mask performance	To assess the mask's performance in relation to leak	
Seal size selection	To assess a way to determine best size of seal for participants	
Anthropometric	To assist with future product development	

8.6. Measurements

[redacted]

[redacted]

[redacted]



[redacted]

8.7. Equipment

Participants will be issued a F&P ICON+ Premo/Auto machine (if required) for baseline data. This device is a market-released device which is supplied with a released user manual. The participants will only be issued an ICON+ device if their current device cannot record efficacy data, leak data or have removable storage (SD card or USB stick).

[redacted]

[redacted]

8.8. Inclusion / Exclusion criteria

Inclusion Criteria

- AHI $\geq$ 5 from the diagnostic night
- $\geq$18 years of age
- Either prescribed APAP, CPAP or Bi-level PAP for OSA
- Existing nasal or nasal pillows mask users (ideally a 70%:30% split)
- Fluent in spoken and written English

Exclusion Criteria

- Inability to give informed consent
- Patient intolerant to PAP
- Anatomical or physiological conditions making PAP therapy inappropriate
- Current diagnosis of respiratory disease or CO_2 retention
- Pregnant or think they may be pregnant

8.9. Point of Enrolment

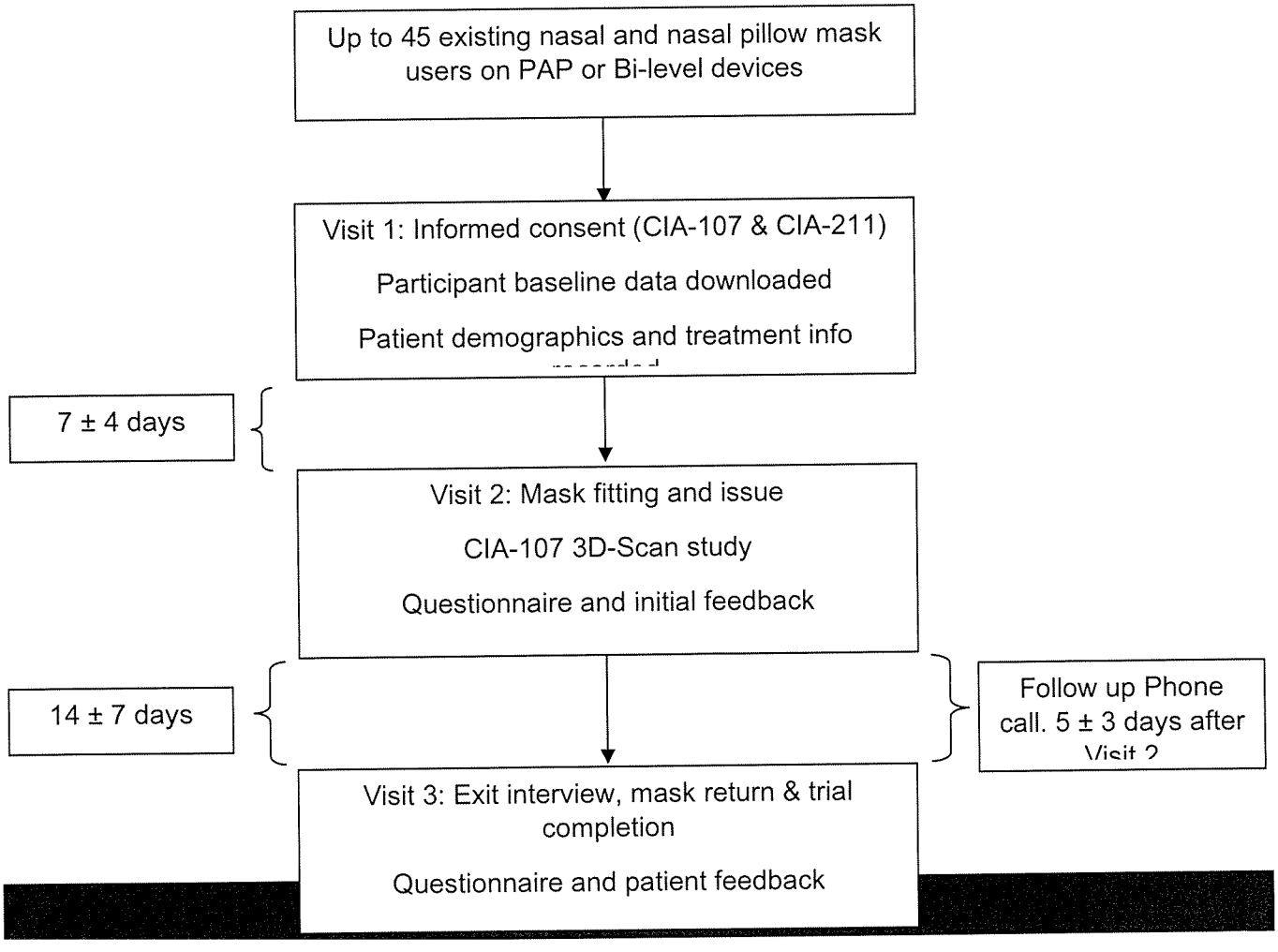
Participants will be recruited from patients who are prescribed either APAP, CPAP or Bi-level PAP for OSA at Clinical Trials of Florida. The principal investigator (or those identified in delegation log) will ask the subjects whether they're interested to take part in the trial. The patients who provide informed consent and meet the inclusion/exclusion criteria will then be enrolled into the trial.

8.10. Patient Procedure

The study coordinator will ask the subjects whether they're interested to take part in the trial. Only eligible participants, that provide written informed consent, will be enrolled into the investigation.

EVENTS	Visit One	Visit Two	Phone Call	Visit Three
Informed consent	X			
ICON+ Premo/Auto given and instructions for use (if applicable)	X			
Commence baseline data gathering	X			

Participant Questionnaire (see Appendix)		X		
Mask fitting with F&P Nasal mask		X		
Head Measurements		X		
Static Leak Measurement		X		
Issue Sleep Diary (Appendix F)		X		
Issue complete Nasal mask with UI		X		
Researcher Questionnaire (see Appendix B)		X		
Baseline PAP device data downloaded		X		
Commence in-home trial of the F&P Nasal mask		X		
Phone call			X	
Return the F&P Nasal mask				X
Returned loaned ICON+ Premo/Auto given and instructions for use (if applicable)				X
Return Sleep Diary				X
Participant Questionnaire (see Appendix)				X
Researcher Questionnaire (see Appendix B)				X
PAP device data downloaded				X



[redacted]

With the following section, the days (± N) reflects: the date that will begin for that section (± the range within which the visit is acceptable).

[redacted]

[redacted]

[redacted]

[redacted]

Clinical Trials of Florida will be providing compensation to the participant of $40.00USD for each completed visit (a total of $120USD for 3 visits). This will be paid after the conclusion of each visit or the withdrawal of the participant from the trial during any of the visits.

8.11. Withdrawal Criteria

Participants will be informed that they have the right to withdraw from the study at any time, without prejudice to their medical care, and are not obliged to state their reasons. The participants are informed that they can revert back to their usual therapy during the clinical investigation if they have reason to do so. Additionally the investigator may withdraw a patient at any time for the following reasons:

[redacted]

[redacted]

- Protocol Violation
- Safety concerns
- Serious illness
- Adverse event

The reason for participant discontinuation in the study is to be recorded in the CRF and source document.

8.12. Number of Trial Subjects

Up to 45 nasal and nasal pillows mask users for OSA therapy will be recruited into this trial.

8.13. Follow up Plan

Patients will receive standard care from their health care provider throughout and following the study.

[redacted]

[redacted]

This is to document that compensation to subjects(s) for trial related injury will be available.

[redacted]

STATISTICAL CONSIDERATIONS

9.5. Description of the Statistical Design

Since the trial is regarding the performance and acceptability of the trial device in order to inform product development, no statistical design is required.

9.6. Sample Size

From the 'Guidance for Industry and Food and Drug Administration Staff – Applying Human Factors and Usability Engineering to Optimize Medical Device Design' document issued on 3 February 2016, a number of 30 users will be sufficient to find a minimum of 97% of problems and on average can find 99% of all problems[13]. Additionally from previous experiences, a number of 30 users was not quite achieved when taking into account drop outs and no shows hence the recruitment drive for up to 45 participants has been set. .

9.7. Pass/Fail Criteria

[redacted]

9.8. Statistical Termination

No interim analysis will be conducted as statistical outcomes will not change the conduct of the study.

9.9. Statistical Procedure Deviations

Statistical procedure deviations will be reported to the principal investigator and the sponsor. Deviations from the original statistical plan will be explained in the final study report.

9.10. Selection Criteria

All participants who consent, and are fitted with a mask that they attempt to sleep on will be included in the analysis. Please see section 8.10 for information on participant flow throughout the trial.

[redacted]

[redacted]

9.11. Statistical Data Management

Fisher and Paykel Healthcare may consult an external statistician to assist with the analysis of the data.

10. Adverse Events and Termination

An Adverse Event (AE) is any adverse change from the participant's baseline condition, i.e., any unfavourable and unintended sign or symptom or disease that occurs during the course of the study, whether or not considered related to the PAP treatment. All clinically significant AEs occurring during the study that were not present prior to the commencement of PAP treatment, will be recorded in the CRF and source document and followed by the Investigator until resolution or stabilization occurs in accordance with GCP.

Serious AE's are considered to be AE's that result in any of the following outcomes, regardless of their relationship to the PAP treatment:

- Death
- A life-threatening AE
- In-patient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- A congenital abnormality/birth defect

[redacted]

[redacted]

Name: Hanie Yee

Address: 15 Maurice Paykel Pl, East Tamaki, Auckland 2013

[redacted]

[redacted]

10.3. Reporting Adverse Events

Any serious AE, due to any cause, that occurs during the study period, must be reported immediately (within the next business day) by telephone to the sponsor. In addition to the initial telephone report, a Serious Adverse Event form must be completed and sent via facsimile to the sponsor. All serious AE's must also be recorded on the AE page of the CRF. Additionally, all serious AE's must be reported to the Independent Review Board (IRB) as per the IRB's requirements.

10.4. Early Termination

The study may be discontinued at any time on the advice of the responsible investigator on the basis of new information regarding safety or efficacy. Additionally, the study may be terminated if progress is unsatisfactory.

The following documentation is required if the appropriate party terminates a clinical trial.

10.5. Investigator

If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution, where required by the applicable regulatory requirements and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.

[redacted]

10.6. Sponsor

If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution, where required by the applicable regulatory requirements, and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.

10.7. Institutional Review Board (IRB)

If the IRB terminates or suspends its approval/favorable opinion of a trial the investigator should inform the institution, where required by the applicable regulatory requirements, and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

11. Publication Policy

This study is intended for internal use on the development of the product. However the results of this study may be used for marketing purposes or in regulatory documentation to support the clinical efficacy of the devices.

12. Approval

All the required signatories for the approval of this document (Clinical Investigation Plan) are listed on the front page of this document with their relevant positions.

13. References

1. Al Lawati N et al. Epidemiology, Risk Factors, and Consequences of Obstructive Sleep Apnea and Short Sleep Duration. Prog Cardiovasc Dis 2009; 51(4): 285-93.
2. Dungan G et al. Randomized Crossover Trial of the Effect of a Novel Method of Pressure Control (SensAwake) in Automatic Continuous Positive Airway Pressure Therapy to Treat Sleep Disordered Breathing. Journal of Clinical Sleep Medicine 2011; 7(3): 261-267.
3. Kribbs NB et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993; 147(4): 887-95.
4. Weaver T, Grunstein T (2008) Adherence to continuous positive airway pressure: the challenge to effective treatment. Proc Am Thorac Soc 15(5):173–178
5. Wolkove N, Baltzan M, Kamel H, Dabrusin R, Palayew M (2008) Long-term compliance with continuous positive airway pressure in patients with obstructive sleep apnea. Can Respir J 15(7):365–369
6. Massie CA and Hart RW. Clinical Outcomes related to Interface type in patients with Obstructive Sleep Apnea/Hypopnea Syndrome who are using Continuous Positive Airway Pressure. Chest 2003; 123:1112-1118.
7. Elliott MW. The Interface: crucial for successful noninvasive ventiolation. European Respiratory Journal 2004; 23:7-8.
8. Schnohofer B and Sortor-Leger S. Equipment needs for noninvasive mechanical ventilation. European Respiratory Journal 2002; 20:1029-1036.
9. Scharf S et al. Racial Differences in Clinical Presentation of patients with Sleep-Disordered Breathing. Sleep and Breathing 2004; 8(4): 173-183.

10. Meetze K et al. Obstructive Sleep Anea: A Comparison of Black and White Subjects. The Laryngoscope 2002; 112(7):1271–1274.

11. Subramanian S et al. Influence of Gender and Anthropometric Measures on Severity of Obstructive Sleep Apnea. Sleep and Breathing 2012; 16(4): 1091-1095.

12. Davidson T, Patel M. Waist Circumference and Sleep Disordered Breathing. The Laryngoscope 2008; 118(2): 339-347.

13. Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and Food and Drug Administration (FDA) staff. Issued on 03 February 2016.

[redacted]

This study will help Fisher & Paykel Healthcare evaluate the performance of the new nasal mask and develop further.

The performance of the Saturn mask will be evaluated by how well it treats your sleep apnea (which is established by the machine data download), your subjective feedback on the performance, comfort and usability of the Saturn mask.

You will be paid $40 for each visit and you will be paid at the conclusion of each visit in the form of a check.

You are eligible to be included in this study if you are:

[redacted]

[redacted]

your consent. You will return the trial mask to the clinical trial staff and this signals the end of the trial participation.

You will be paid $40 for each visit after the conclusion each visit in the form of a check. You are free to withdraw from the trial at any time and it will not affect your healthcare or any chance of participating in future trials. If you are withdrawn from the trial, you will be paid for the number of visits you made to the healthcare center.

[redacted]