Fisher & Paykel
HEALTHCARE

Clinical Investigation Plan: [redacted]

Document No.	Rev	Document Title (must be the same as Database/ hardcopy)	Category-Folder (e.g. DHF)	Folder No.	Folder Tab section
CIA-176	**B**	**Clinical Investigation Plan:** [redacted]	**CIA**	**176**	**2.4**
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Review and Approval

Please tick if task complete:	Pre-release database done ☐, File(s) in DRAFT & Closed ☐

[redacted]

Irene Cheung
Author

[redacted]

[redacted]

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[redacted]

[redacted]

1. Revision History

Revision	Author	Date	Description of change
A	Irene Cheung	12 April 2016	First release
B	Irene Cheung	21 June 2016	Administrative changes to the questionnaire in Appendix A and B Changed sponsor contact person to Hanie Yee (Clinical Research Manager) Changed reporting of adverse events to Hanie Yee (Clinical Research Manager)

2. List of Abbreviations

AutoCPAP	Auto-adjusting Continuous Positive Airway Pressure
CIP	Clinical Investigation Plan
CPAP	Continuous Positive Airway Pressure
CRF	Case Report Form
FPH	Fisher & Paykel Healthcare
HIPPA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
IRB	Institutional Review Board
OSA	Obstructive Sleep Apnea

3. Document Information

3.1. Purpose and Scope

This clinical investigation plan (CIP) is compiled by the investigators and sponsor (Fisher & Paykel Healthcare (FPH)). The CIP is designed to optimize the scientific validity and reproducibility of the results of this study in accordance with current clinical knowledge and practice so as to fulfil the objectives of the investigation. The investigator and the sponsor will store the current copy and all previous copies of the CIP.

The purpose of the clinical investigation, [redacted] is listed in Section 8 Objectives of the Clinical Investigation.

3.2. 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.

3.3. Persons Authorized to Amend the CIP

[redacted]

3.4. Monitoring Arrangements

[redacted]

[redacted]

[redacted]

The details can be found in the monitoring plan.

3.5. Data Management

[redacted]

4. Investigator Information

4.1. Study Principle Investigator

Name: Matt Uhles
Address: Clayton Sleep Institute[redacted]
Email: uhlesm@claytonsleep.com
Phone: 314-645-6005

[redacted]

4.1.1. Co-ordinating Investigator

Name: Angela Lindsey
Address: Clayton Sleep Institute[redacted]
Email: LindseyA@claytonsleep.com
Phone: 314-645-6005

[redacted]

4.2. Investigators

[redacted]

4.2.1. Co-ordinating Investigator

[redacted]

4.3. Investigators

[redacted]

[redacted]

4.3.1. Co-ordinating Investigator

[redacted]

4.4. Investigators

[redacted]

4.4.1. Co-ordinating Investigator

[redacted]

4.4.2. Co-ordinating Investigator

[redacted]

4.5. Other Investigators

[redacted]

4.6. Institution

[redacted]

[redacted]

[redacted]

[redacted]

5. Sponsor Information

5.1. Primary Sponsor Details

Name of Business: Fisher & Paykel Healthcare Limited
Address: 15 Maurice Paykel Place, East Tamaki, Auckland, New Zealand.

[redacted]

6. Device Information

6.1. Identification of the Medical Device

[redacted]

The investigational device will provide continuous positive airway pressure to the participant via a breathing tube and interface (mask). [redacted]

[redacted]

[redacted]

6.2. Device Risk Analysis and Management

All investigational devices used in this clinical investigation will undergo device risk analysis and management prior to being released for clinical investigation. Evidence of the risk management process will be filed in the Clinical Investigation Folder (CIA-176).

All contraindications, warnings, precautions and adverse effects of using this device are included in the device manuals, filed in CIA-176, [redacted].

Reporting of adverse events or adverse device effects will be included in the Clinical Investigation Folder (CIA-176), the site regulatory file and reported on the participant's case report form (CRF).

7. Justification for a Clinical Trial

7.1. Synopsis

Existing and Naïve CPAP users will be recruited into this [redacted] study to evaluate the clinical performance [redacted]

[redacted]

[redacted]

7.2. Literature Review

Obstructive sleep apnea (OSA) is a prevalent health issue in western world effecting 24% of men and 9% of women of the middle age population, and affecting around 2-4% of the total adult population [1, 2]. It is characterized by periodic collapse of the upper airway during sleep. CPAP is the primary treatment for patients with OSA[3,4]. [redacted]

[redacted]

[redacted]

7.3. Preclinical Testing

[redacted]

7.4. Previous Clinical Experience

[redacted]

[redacted]

7.5. Justification for Administration

The device, [redacted] used in this trial have been previously tested [redacted]

[redacted]

8. Objectives of the Clinical Investigation

8.1. Hypothesis

The [redacted] investigational device clinical performance will be acceptable in terms of product reliability, therapy effectiveness and user feedback.

8.2. Objectives

The primary objective for this investigation is to evaluate whether the investigational device treats the participant safely, effectively and reliably [redacted]

[redacted]

The secondary outcome of this investigation is the participant perception of the device through the participant perception questionnaire, [redacted]

8.3. Population

This investigation will include a total of 150 adult participants (22 or older) with a diagnosis of OSA and a PAP (CPAP or AutoCPAP) prescription. They may be either experienced users of PAP or naïve to PAP therapy. Further details are included in Section 9.8 Inclusion/Exclusion Criteria.

8.4. Risks

Positive airway pressure therapy is considered to be the gold-standard therapy for individuals with OSA (Section 7.2). The treatment is considered to be extremely safe and any adverse effects are usually short term and easily resolvable. Adverse effects can be caused by an ill-fitting mask, too much or too little pressure being delivered to the participant, existing or developing nasal congestion during CPAP use. Individuals that are contraindicated for CPAP therapy will be excluded during screening. For more information on contraindications, warnings and precautions refer to the user manuals provided in CIA-176, [redacted].

The primary risk within the scope of this study that the pressure may be slightly too high or slightly too low [redacted]

[redacted]

[redacted] In the case of the pressure being slightly too low (sub-therapeutic), this may result in the participant having sleep disordered breathing events. If the pressure is too high, then the participant may be uncomfortable during CPAP use. Either of these may result in the participant feeling more tired than usual the next day. Other risks [redacted] side effects of CPAP related to nasal dryness and congestion. All of these risks are common to [redacted] CPAP devices, and this study represents no greater risk than usual therapy.

[redacted]

8.5. Essential Requirements of the Relevant Directive

[redacted]

9. Clinical Investigation Design

9.1. 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 [redacted] will not be randomized [redacted]

9.2. Controls

No control group will be used in this study [redacted]

9.3. Bias

Participants will not be blinded to any therapy settings for the duration of the trial. [redacted]

9.4. End Points

9.4.1. Primary Outcomes

The primary outcomes of effectiveness, safety and reliability will be measured by:

[redacted]

9.4.2. Secondary Outcomes

The secondary outcome of this investigation is the participant perception of the device [redacted]

9.5. Variables

The following variables will be recorded during the investigation:

[redacted]

[redacted]

9.6. Measurements

The following measurements will be performed during the study [redacted]

[redacted]

9.7. Equipment

Each participant will be issued the following:

[redacted]

9.8. Inclusion / Exclusion criteria

The inclusion criteria for participants in this investigation will be:

- Aged 22 and over (FDA defined as adult).
- Diagnosed with OSA by a practicing physician and prescribed PAP (CPAP or AutoCPAP) therapy.

[redacted]

- For experienced users of PAP (CPAP or AutoCPAP):
    - Using the PAP of more than 4 hours/night for 70% during the last 30 days (justification allowed by the investigator of each site if the participant does not meet this compliance but is deemed suitable for this trial).

The exclusion criteria for participants in this investigation will be:

- Contraindicated for PAP (CPAP or AutoCPAP) therapy.
- Persons with other significant sleep disorder(s) (e.g. periodic leg movements, insomnia, central sleep apnea).
- Persons with obesity hypoventilation syndrome or congestive heart failure.
- Persons that require supplemental oxygen with their PAP (CPAP or AutoCPAP) device.
- Persons with implanted electronic medical devices (e.g. cardiac pacemakers).
- Persons who are pregnant or think they might be pregnant.
- Persons whose is not fluent in spoken and written English.

9.9. Point of Enrolment

A participant shall be considered enrolled into the investigation once they have been screened for the inclusion/exclusion criteria, signed the informed consent form and taken the device home to use for the first time.

9.10. Patient Procedure

[redacted]

[redacted]

9.11. Withdrawal Criteria

Participants enrolled in this investigation will be notified that they have the right to withdraw from the investigation at any time, without prejudice to their medical care and are not obliged to state their reasons. The investigator will follow-up any withdrawals.

Additionally, the investigator may withdraw a participant at any time for the following reasons:

1. Inability to tolerate trial PAP device due to nasal obstruction or claustrophobia
2. Protocol violation
3. Serious illness
4. Adverse events

The reason for participant discontinuation in the investigation is to be recorded in the CRF and will be included in any clinical investigation report.

[redacted]

9.12. Number of Trial Subjects

150 trial participants will be included in this investigation, [redacted]

[redacted]

9.13. Follow up Plan

[redacted]

Participants remain under the medical care of their usual care provider during the trial, and after the trial has concluded.

9.14. Foreseeable Complications

PAP [redacted] use may irritate certain conditions and may be temporarily contraindicated in participants who exhibit sinus infection, middle ear infection or a perforated ear drum. Participants that are contraindicated for PAP [redacted] will be excluded from the investigation.

The participant will be instructed to cease using the device if they think the device is malfunctioning, not treating them or if they feel uncomfortable using the device; and that they should immediately swap to their usual PAP device (if available) for the rest of the night and contact a member of the research team as soon as possible. The research team will then assess with the participant if the problem can be resolved, or withdraw them from the trial.

10. Clinical Trial Documentation

10.1. Consent and Recruitment

Informed consent will be taken for all participants enrolled in this investigation. A copy of the information sheet and consent form is included with the ethics application, [redacted]

10.2. Case Report Form

Investigation data will be recorded in source documents and attached to the Case Report Form (CRF) for both the administration of the investigation and collection of participant data. [redacted]

10.2.1. Case Report Form Signatories

Case Report Form Signatories will be included on the Delegation of Authority in the site regulatory file.

10.3. Insurance Statement

A copy of the insurance statement will be included in the CIA folder [redacted].

[redacted]

10.4. Record of Deviations

There are currently no deviations to the clinical investigation plan (CIP).

STATISTICAL CONSIDERATIONS

10.5. Description of the Statistical Design

[redacted]

[redacted]devices is based upon a binomial model of 90% confidence and 99% reliability, [redacted] Refer to 10.7 Pass/Fail criteria for description and classification of failures.

10.6. Sample Size

150 participants will be required as part of this [redacted] assessment [redacted]

[redacted]

10.7. Pass/Fail Criteria

[redacted]

[redacted]

[redacted]

10.8. Statistical Termination

There is no criteria for statistical termination for this investigation.

10.9. Statistical Procedure Deviations

There is no criteria for statistical procedure deviations for this investigation.

10.10. Selection Criteria

[redacted]

10.11. Statistical Data Management

[redacted]

11. Adverse Events and Termination

11.1. Emergency Contact Details

The participant will contact their following investigator if there are any adverse events:
Name: Matt Uhles
Address: Clayton Sleep Institute, [redacted]
Email: uhlesm@claytonsleep.com
Phone: 314-645-6005

[redacted]

[redacted]

11.2. Foreseeable Adverse Events

Foreseeable adverse events for this investigation include the following:

[redacted]

These foreseeable adverse events are the same as those for a PAP patient on their usual therapy.

11.3. Reporting Adverse Events

[redacted]

11.4. Early Termination

If a participant is struggling with therapy during the investigation and we are unable to resolve the issue causing the problem, the participant may be terminated early from the investigation. The participant also has the right to withdraw from the investigation at any point without a need for a reason.

If [redacted] it becomes clear that the [redacted] device is not treating participants effectively, the investigator may terminate the trial in its entirety.

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

11.4.1. 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.

11.4.2. 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.

11.4.3. 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.

12. Publication Policy

[redacted]

13. Approval

Signing the below approval indicates that the principal investigator(s) (PI) in each trial center and the sponsor agree to this version of Clinical Investigator Plan.

Principal Investigator Approval:

PI Name: _____

PI Signature: _____

Date (dd/mmm/yyy): _____

Sponsor Approval

Sponsor Name: _____

Sponsor Signature: _____

Date (dd/mmm/yyy): _____

14. References

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]