Clinical Investigation Plan

F&P Toffee Nasal Pillows Mask, US, 2022

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NCT05573763	**A**	**Clinical Investigation Plan F&P Toffee Nasal Pillows Mask, US, 2022**	**18 Oct 2022**
Additional copies to:			
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Review and Approval

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Name	Title	Signature	Date
[redacted]	[redacted]	Refer to supporting documents for electronic approvals as per [redacted] Dated 18 Oct 2022	
[redacted]	[redacted]		
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[redacted]	[redacted]		

Contents

1. Revision History

Rev	Date	Author	Description of Changes
A	18 October 2022	[redacted]	First issue.

1.1. List of Terms

Abbreviation	Definition
AE	**Adverse event** Any untoward medical occurrence, unintended disease, or injury, or clinical signs, including abnormal laboratory findings, among participants enrolled in the clinical investigation, regardless of if they arise due to use of the investigational product. *See also: SAE*
AHI	**Apnea-Hypopnea Index** Measure of sleep apnea severity calculated from the number of apneic and hypopneic episodes combined per hour of sleep which last more than 10 seconds and are associated with a decrease in blood oxygenation.[1]
APAP	**Auto-titrating positive airway pressure** Mode of non-invasive ventilation during which a low set pressure is supplied to the airway, unless an obstruction is detected, in which case this ramps up to a higher pressure.[1]
BPAP	**Bi-level positive airway pressure** Mode of non-invasive ventilation during which two distinct pressures, one at inhalation and the other at exhalation, are supplied to the airway.[1]
[redacted]	
CIA	**Clinical Investigation Administration** Physical and electronic folder which corresponds to a unique identification number created by F&P for clinical investigations, to house relevant contracts, documentation, and memos.
CIP	**Clinical Investigation Plan** Document that states the proposed rationale, objectives, design, methodology, monitoring, organization, conduct, statistical considerations, analysis, and record-keeping for an intended clinical investigation.
CMD	**Clinical Master Data** A compilation of up-to-date clinical data related to a therapy and associated medical procedures which is generated using a comprehensive search protocol and appraisal strategy.
CPAP	**Continuous positive airway pressure** Mode of non-invasive ventilation during which a fixed pressure with constant flow is supplied to the airway during inhalation and exhalation.
CRF	**Case Report Form** Deidentified document used by research personnel carrying out a clinical investigation to record source information relating to a participant, including data which is collected and procedures that are followed.

CTA	**Clinical Trial Agreement** Formal contract between the sponsor organization and investigation site outlining the roles and responsibilities for both parties conducting the clinical investigation.
DHF	**Design History File** Compilation of documentation that describes the design and development history of the investigational product.
DOA	**Delegation of Authority** Document which defines, establishes, and allocates all functions and duties to be carried out by research personnel as part of the clinical investigation.
DR	**Design Review** Milestone in the development process of the investigational product, whereby a design is evaluated against its requirements to verify outcomes of previous activities or identify issues.
ESS	**Epworth Sleepiness Scale** A self-administered questionnaire used to indicate the risk of an individual dozing in specific situations, which can be used to estimate levels of excessive daytime sleepiness.[1]
FDA	**Food and Drug Administration**
F&P	**Fisher & Paykel Healthcare Ltd.**
GCP	**Good Clinical Practice** Standard which forms an integral part of ISO 14155:2020, for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical investigations that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of participants has been preserved.
HA	**Hazard Analysis** Assessment of risk based on identifying hazardous situations which may affect the overall safety or quality of the investigational product, so they can be controlled or eliminated.
IB	**Investigator's Brochure** Compilation of the clinical and non-clinical data available on the investigational product which is being tested or used during the clinical investigation.
ICF	**Informed Consent Form** Document which thoroughly outlines what to expect during the clinical investigation, including procedures, risks, benefits, reimbursement, confidentiality, privacy, contacts, and information about the sponsor organization and investigation site for prospective participants to review, in addition to a section wherein enrolment can be confirmed should they agree to the terms.
ICH	**International Conference on Harmonization** Global body comprised of representatives from various national standards organizations, intended to promote worldwide proprietary, industrial, and commercial standards.
IPAP	**Inspiratory positive airway pressure** Pressure which forces air into the lungs applied during the inspiratory breathing phase of invasive ventilation or NIV.[1] *See also: BPAP*
IRB	**Institutional Review Board** Independent ethics committee responsible for reviewing specific details of the clinical investigation protocol prior to it being administered so that the rights, safety, and wellbeing of recruited human subjects is protected.

ML	**Monitoring Log** Record of monitoring activities and deficiencies in clinical investigation documentation completed by an appointed monitor, to ensure progress and processes being conducted are recorded and reported in accordance with the CIP, as well as applicable ethical guidelines and regulatory requirements.
NIV	**Non-invasive ventilation** Airway support administered through a mask wherein inhaled gases are supplied with positive end-expiratory pressure, often at a set tidal volume and rate.[1]
NZ	**New Zealand**
OHS	**Obesity hypoventilation syndrome** Sleep-related disorder accompanied by severe overweightness, hypoxemia during sleep, and hypercapnia during the day, resulting from excessively slow or shallow breathing.[1]
OSA	**Obstructive sleep apnea** Sleep-related disorder characterized by recurrent interruptions in breathing during sleep due to temporary obstruction of the airway by lax, excessively bulky, or malformed pharyngeal tissues, with resultant hypoxemia and chronic lethargy.[1]
[redacted]	[redacted]
PAP	**Positive airway pressure** Mode of respiratory ventilation during which compressed air is supplied to the lungs to prevent episodes of airway collapse and to facilitate normal breathing.[1]
[redacted]	
PDP	**Product Development Plan** Document covering a broad set of execution and control stages within a project, including considerations for risk management, verification, and clinical validation for the investigational product.
PI	**Principal Investigator** Qualified and certified individual responsible for overseeing and conducting the clinical investigation at an investigational site.
PR	**Pressure relief** Provides a brief and small pressure drop during the later stages of inspiration and the onset of exhalation, before returning to the set treatment pressure. The magnitude of any given pressure drop can vary on a breath-by-breath basis, and depends on actual airflow, and is intended to reduce the sensation of breathing against high pressure without causing the upper airway to collapse.[1]
PTX	**Product Traceability Matrix** Describes the technical specifications and user requirements for a given test scenario or task as part of developing the investigational product.
RR	**Reimbursement Register** Record of remuneration issued to participants during the clinical investigation.
RS	**Recruitment Script** Standardized text research personnel use during the recruitment phase to disclose important aspects of the clinical investigation to potential participants.

SAE	**Serious adverse event** AEs that result in death, congenital anomalies, or birth defects, or that which require either inpatient or prolongation of hospitalization, are life-threatening, or result in a persistent or significant disability or incapacity. *See also: AE and SAEF*
SAEF	**Serious Adverse Event Form** Records specific details and tracks the outcome of any adverse event considered serious that affect participants in the clinical investigation. *See also: SAE*
SIL	**Subject Identification Log** Record of subject allocation to a random identification number.
SP	**System Procedure** Defines how the requirements of individual elements of a management standard are implemented at F&P.
TP	**Test Protocol** Outlines details of the methodology and procedures to be carried out to evaluate specific objectives or answer a research question.
TR	**Test Report** Results from a specified set of testing based on the scope of a corresponding protocol, including any deviations and analysis of acceptance thresholds for each requirement being evaluated.
UI	**User Instructions** Document supplied with the investigational product that outlines appropriate use and maintenance, alongside any relevant warnings and cautions for operation.
US	**United States**

2. Document Information

2.1. Purpose and Scope

The purpose of this Clinical Investigation Plan (CIP) is to outline the proposed [redacted] associated with the intended clinical investigation. This document has been compiled by the sponsor organization, Fisher & Paykel Healthcare Ltd. (F&P), located in New Zealand (NZ), in collaboration with the investigation site, [redacted] to provide all research personnel with sufficient information to complete protocol procedures to an acceptable standard, [redacted]

This protocol has been designed in such a way as to optimize the [redacted] This includes considerations to minimize pain, discomfort, fear, and any other foreseeable risks as much as possible for participants. The clinical investigation shall comply with all relevant recognized ethical principles involving humans participating in medical device research, including ISO-14155: 2020, the Declaration of Helsinki, and applicable International Conference on Harmonization (ICH) Good Clinical Practice (GCP) principles. Where there are deviations from GCP E6:R2 in requirements or terminology in comparison to ISO-14155:2020, ISO-14155:2020 will take precedence. For example, the term "legally designated representative" from ISO-14155:2020, compared to "legally acceptable representative" from GCP E6:R2. No deviation from the clinical investigation protocol will be implanted without prior review and approval from F&P, except where it may be necessary to eliminate an immediate hazard to a participant. In such case, the protocol deviation or protocol violation will be reported to F&P as soon as possible.

[redacted]

2.2. Confidentiality Statement

This CIP contains commercially sensitive and confidential information belonging to F&P and is provided for the sole purpose of enabling an evaluation of a possible collaboration between F&P and the investigation site to undertake the proposed clinical investigation for the investigational product. As such, this CIP must remain confidential at all times, and any disclosure, distribution, or reproduction of this CIP beyond its intended purpose is strictly prohibited.

2.3. Document Amendments

Only the below persons, in addition to the individual listed as the author, are permitted to amend this CIP.

Name	Designation	Role
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

3. Investigation Site Information

3.1. Principal Investigator

Name	[redacted]
Institution	[redacted]
Designation	[redacted]
Address	[redacted]
Phone	[redacted]
Email	[redacted]

3.2. Investigation Site Representative

Name	[redacted]
Institution	[redacted]
Designation	[redacted]
Address	[redacted]
Phone	[redacted]
Email	[redacted]

4. Sponsor Information

4.1. Primary Sponsor Representative

Name	[redacted]
Institution	F&P
Designation	[redacted]
Address	[redacted]
Phone	[redacted]
Email	[redacted]
Residence	NZ

Responsibilities	Ensuring quality management processes and procedures are followed, carrying out the monitoring plan, assisting with provision of investigational product, documenting significant protocol exemptions, as well as selecting and training research personnel.

4.2. Overseas Sponsor Representative

Name	[redacted]
Institution	F&P
Designation	[redacted]
Address	[redacted]
Phone	[redacted]
Email	[redacted]
Residence	[redacted]
Responsibilities	Local contact that facilitates correspondence and communication with investigation site on behalf of the sponsor representative, as well as overseeing the logistics of transporting investigational product to and from the investigation site.

5. Clinical Investigation Justification

5.1. Clinical Investigation Agreements

A formal contractual clinical trial agreement (CTA) shall be in place with [redacted] prior to the commencement of this clinical investigation. This agreement covers the relevant costs for each procedure conducted by the investigation site and any overarching costs, such as overhead or room hire, with respect to the requirements stipulated in this CIP. A copy of the fully executed CTA is filed within [redacted]

5.2. Clinical Investigation Financing

All costs and expenses for this clinical investigation shall be covered by the F&P, [redacted] As a requirement for conducting this clinical investigation in line with ISO-14155:2020, F&P will ensure a valid insurance certificate is provided to cover any unanticipated costs. [redacted]

5.3. Training Sessions

The PI and all research personnel appointed as a [redacted] CRCs and Product Development (PD) staff from F&P who will be facilitating aspects of the clinical investigation or completing monitoring will also receive training. While the first training session will provide a brief introduction to the investigational product, an overview of the clinical investigation timeline, as well as an in-depth explanation of the protocol procedures to be carried out at each phase, the second session will more comprehensively cover the key features of the investigational product, how to clean it, assemble and disassemble it, and fit and remove it. The second session will also explain how to

conduct necessary safety checks on the investigational product before it is issued to participants, in addition to any recommendations for troubleshooting should participants have any issues. [redacted]

5.4. Research Purpose

This clinical investigation is designed to validate and confirm the overall performance and acceptability of the [redacted] prior to its global commercial release, serving as the final pre-market assessment to ensure the investigational product, when used according to its intended purpose, provides positive airway pressure (PAP) therapy for existing patients which is equivalent to the treatment provided by their usual mask. Nasal pillows masks, such as the [redacted], are commonly used as part of PAP therapy, both in clinical settings and in-home environments for the treatment of various respiratory conditions, including obstructive sleep apnea (OSA). Currently, as per ISO-14155:2020, '*Annex I*', the [redacted] is considered in the pivotal stage of device development.

[redacted]

5.5. Pre-clinical Testing

PAP therapy is a treatment designed to be administered to humans. There are currently no generally accepted pre-clinical testing practices that can be carried out for the medical device being used in this clinical investigation, [redacted] Therefore, these features of PAP therapy masks make any pre-clinical testing on non-humans inappropriate for the development of the medical device. However, a series of bench tests is conducted on the investigational product to ensure it is safe and will perform as expected when used on human subjects. [redacted]

5.6. Literature Review

A full description of PAP therapy and the clinical indications for which it is prescribed or administered to treat is provided in the [redacted]

PAP and non-invasive ventilation (NIV) are common treatments used in chronic care to assist in airway management for several respiratory conditions present in both adults and adolescents, including OSA and obesity hypoventilation syndrome (OHS). The prevalence of these conditions continues to rise as noncommunicable diseases, such as obesity, become more common across many parts of the world.[2,3] Historically, invasive methods of ventilation were required to maintain airway patency, but this is often associated with significant long-term medical complications as well as increased susceptibility to other conditions.[4] Non-invasive methods, if appropriate for a patient, are now more appealing to practicing physicians, especially if treatment is administered in a non-clinical setting, such as the home. PAP therapy was first described in 1981 for the treatment of OSA, a form or sleep-disordered breathing characterized

by upper airway collapse during sleep.[5] PAP therapy is now a well-established, effective, and the clinically preferred treatment for OSA, helping resolve many of the primary markers of disease severity. It has evolved to include a variety of modes including APAP, BPAP, and CPAP, as well as comfort features such as humidification and pressure relief (PR) which appear to improve initial uptake as well as long-term adherence among those prescribed with the treatment.[1] PAP therapy is delivered through a system of components which includes a flow generator, breathing tube, and mask, sometimes with the addition of a humidifier or mask accessory.

[redacted]

It is generally accepted, based on consensus in the research literature, that PAP therapy:

- Is safe to use among adults with OSA
- Reduces Apnea-Hypopnea Index (AHI) and excessive daytime sleepiness among adults with OSA
- Reduces AHI among adults with OHS
- In the form of APAP and CPAP are equally efficacious for treating adults with OSA

[redacted]

PAP and NIV therapies are still considered the most effective and reliable treatment options for those with OSA and OHS, despite advancements in alternative treatments, such as oral appliances and surgical interventions to remodel structures at the back of the throat, including tonsillectomies or uvulopalatopharyngoplasty.[4,6] Professional organizations continue to recommend PAP or NIV therapy, where applicable and appropriate, over alternative treatments. To deliver effective therapy, the components which make up the treatment system must work harmoniously. While the effective pressure is determined by a practicing physician, the machine which generates flow must accurately and consistently deliver required prescribed constant or fluctuating pressures. The intended purpose of the mask component of the PAP therapy system is to provide effective fit and seal within the nostrils, around the nares, or over the nose and mouth. Masks should be suitable for use in a home environment or any setting where a patient may sleep, and may be used by a wide range of people with varying expertise and education, ranging from patients with limited or no knowledge and experience, to qualified healthcare professionals who will prescribe or recommend PAP therapy.

As the mask maintains the seal between the patient and the device to ensure adequate and continuous delivery of the prescribed therapeutic pressure, unintentional leak from the interface should remain relatively low, given even

minor levels of leak can significantly impact the sleep quality and level of comport experienced by patients using PAP therapy. This in turn, may impact their long-term tolerance and adherence to treatment.[1,7] It is important to note that masks are designed to have a certain acceptable level of unintentional leak, depending on the pressure prescribed for a patient, and mask seal size, as the interface will contain holes to allow for exhaled carbon dioxide flushing. Although published literature does not define an acceptable level of leak, it is understood that as leak increases, the overall experience deteriorates and treatment benefit observed in patients will likely decrease. Masks will typically have a manual method of adjustment to help patients obtain a comfortable or customized fit against the face, and are usually available with multiple headgear or cushion sizes to accommodate patients with different craniofacial features.

While there are a significant number of benefits to using PAP and NIV therapies for the relevant indications, both also come with some risks to the patient. These include potential sleep disruption, facial irritation, mandibular pain, internal trauma, anxiety sensitivity, abdominal discomfort, physiological compromise, facial discomfort, facial dryness, mucosal congestion, and facial inflammation.[8–10] However, manufactures of medical devices which deliver PAP and NIV therapies can address a number of these side effects by improving design and functionality. This may involve the incorporation of humidification and PR technologies in devices, or the use of comfortable and non-irritating materials for masks.

6.

7. Investigational Product

7.1. Identification of the Medical Device

A full description of the investigational product, [redacted]

[redacted]

[redacted]

7.2. Intended Use

[redacted]

7.3. Device Risk Analysis and Management

PAP therapy is currently one of the least invasive and most widely recommended treatments for OSA, and serves as the generally accepted state of the art within the field of sleep and respiratory medicine. The acceptability of risk associated with PAP therapy devices, interfaces, accessories, and supporting information technology for delivering treatment to the target population are shared, and is appropriate, as the benefits of PAP therapy outweigh most risks.

[redacted].

7.4. Previous Clinical Experience

[redacted]

[redacted].

[redacted]

[redacted]

7.5. Essential Requirements of Relevant Directives

[redacted]

7.6. Justification for Administration

There is an ongoing need for advancement in design and technology for PAP therapy masks on the market, specifically as a means of improving comfort for patients and encouraging long-term adherence to treatment.

[redacted]

7.7. Investigational Product Lifecycle

[redacted]

8. Monitoring Arrangements

8.1. Monitor Responsibilities

[redacted]

Clinical investigation monitoring will include source data verification by a legally designated representative, in addition to a review of Informed Consent Forms (ICF), protocol deviations or violations if present, recording and reporting of adverse events that occur during the clinical investigation, and the regulatory binder possessed by the investigation site. As part of this clinical investigation, data may be recorded in a variety of ways, including clinical records, feedback forms, and information recorded on the Case Report Form (CRF) based on direct observation. Any clinical data recorded directly onto the CRF shall constitute source data. Corrections shall be made in such a way as to be compliant with Good Document Practice, with a single line through the error, alongside the initials of the individual making the change that can be matched to the DOA, the date of change in the DD/MMM/YYYY format, and justification for the change.

The arrangements outlined will be agreed upon and approved by F&P and the appointed clinical monitor prior to commencing the clinical investigation. Persons appointed to monitor the progress of this clinical investigation, as identified in the DOA, and PI will have access to all source documents needed to verify entries into CRF, as well as

other documentation, provided participant confidentiality is maintained in accordance with local regulations. It will be the responsibility of the PI and CRC from F&P to inspect CRFs at regular intervals over the duration of the clinical investigation, to verify adherence to the protocol specified in this CIP, and to ensure the correctness and comprehensiveness of all data being entered into clinical investigation-related documentation. Additionally, F&P will undertake at least one monitoring session while the clinical investigation is active, and at least one monitoring session upon completion of the clinical investigation. These monitoring activities may be conducted in-person, remotely, or a combination of both. The investigation sites will be informed of this prior to any monitoring taking place. All [redacted]

The monitor will be required to have in depth knowledge of this CIP, regulatory requirements, and any relevant system procedures (SP) at F&P. Relevant qualifications and experience should be listed in the curriculum vitae of the monitor. It is essential that the monitor has not conducted any prior data entry procedures for the CRFs or ICFs they [redacted]

[redacted]

8.2. Site Monitoring Schedule

A minimum of [redacted]

Details of each visit are as follows:

[redacted]

[redacted]

At this visit, the monitor will:

- Ensure any queries are resolved, CRFs are completed to a suitable standard and appropriately filed, issues are addressed, and all investigational product is accounted for
- Review regulatory binder

8.3. Data Management

Results as part of this clinical investigation will be stored in the F&P controlled documents system [redacted]

All participants will be provided with a signed ICF copy before protocol procedures commence. [redacted]

[redacted]

8.4. Clinical Investigation Identifier

This clinical investigation will be identified by [redacted] Furthermore, details of this clinical investigation will be submitted online to ClinicalTrials.gov to fulfill the registration requirement as per ISO-14155:2020, with the associated National Clinical Trial number generated through registration referenced [redacted]

9. Clinical Investigation Objectives

9.1. Research Hypotheses

[redacted]

9.2. Primary Objective

[redacted]

9.3. Investigational Endpoints

[redacted]

[redacted]

9.5. Sample Size

[redacted]

[redacted]

[redacted]

9.6. Participant Population

[redacted] will recruit between 40 and 45 male and female adult participants who have been prescribed PAP therapy for the clinical investigation [redacted]

9.7. Enrolment Eligibility

Below are the inclusion criteria for enrolment in the clinical investigation:

- Persons who are ≥22 years of age
- Persons who weigh ≥66 pounds
- Persons who have been prescribed PAP therapy by a physician
- Persons who are existing nasal pillows mask users with ≥3 months of use prior to enrolment in the clinical trial
- Persons who are compliant with PAP therapy for ≥4 hours per night for ≥70% of nights for a 14-day period within 30 days prior to enrolment in the clinical trial
- Persons who are fluent in spoken and written English
- Persons who possess the capacity to provide informed consent

Below are the exclusion criteria for enrolment in the clinical investigation:

- Persons who are intolerant to PAP therapy
- Persons who possess, or suffer from, anatomical or physiological conditions which make PAP therapy inappropriate
- Persons who are required to use PAP therapy for >12 hours per day or for extensive periods, not including sleep or naps
- Persons who are trying to get pregnant, are pregnant, or think they may be pregnant
- Persons who have an IPAP pressure of >25 cmH_2O if on BPAP
- Persons who use a PAP therapy device for the delivery of medicines, except supplemental oxygen
- Persons who use a PAP therapy device that does not possess data recording capabilities to capture AHI and a numerical indicator of leak that is accessible to the investigation site

[redacted]

9.8. Vulnerable Populations

There is no intention to recruit individuals in vulnerable populations. More specifically, children or minors, and pregnant women, are expressly excluded from this clinical investigation. However, it is important to note that it is expected that a proportion of the sample population will be considered elderly or immunocompromised, as these individuals would generally constitute a large proportion of the PAP therapy user population. There will be no direct health-related benefit to this subgroup of the overall sample. PAP therapy does not serve as treatment for a health

problem specific to the elderly or immunocompromised, but it is imperative to ensure that the investigational product can be used effectively in this population. Therefore, recruitment will not specifically target this population, but will not exclude them from the sample should they meet the inclusion and exclusion criteria. There are no additional risks posed to elderly or immunocompromised participants that they are not already exposed to as routine users of PAP therapy.

9.9. Risks and Benefits

PAP therapy is considered standard treatment for the management of OSA. The risks associated with this treatment are limited to potential minor discomfort associated with using any type of PAP therapy mask during sleep, as documented in [redacted] There will be no additional risks to participants undergoing the intervention over the course of this clinical investigation, as participants will be following routine practice for management of their diagnosed medical condition. Participants in the clinical investigation may benefit from receiving additional follow-up during appointments at [redacted], or advice regarding sleep disorders or PAP therapy. [redacted]

10. Clinical Investigation Design

10.1. Study Design

[redacted]

10.2. Controls and Bias

No control group will be used in the clinical investigation as it is designed to test the [redacted] the investigational product against product requirements, and potentially to inform future product development with findings. However, participants using specifically targeted released PAP therapy masks that are available to purchase on the market will enrolled in the clinical investigation to fulfil the primary recruitment goals and provide comparison to the [redacted]. Therefore, while this is not a formal control group, there is a degree of control for comparison.

The investigational product is distinguishable and will be labelled with identifying features. Since the investigational product being tested is the same for the entire sample population, the clinical investigation will not be blinded. All participants recruited for this clinical investigation will receive a [redacted] for use in the home. Thus, there is only one treatment group and there will be no randomization as there is no intention to make comparisons between any treatment groups. Data collected across several research variables for this clinical investigation is qualitative in nature or self-reported. Where possible, objective and validated measurement tools have also been included to corroborate or elucidate any bias, or challenge and confirm conflicting or inconsistent data.

10.3. Data Collection

[redacted]

[redacted]

Treatment efficacy data will be derived from AHI and leak information in compliance reports, as collected by [redacted] during recruitment, [redacted] and prior to the [redacted]. Baseline data will be downloaded for a two-week period within 30 days prior to enrolment, and investigational data will be downloaded for all nights from Visit 1 to the night before participants attend [redacted] To mitigate any risks associated with introducing another potential extraneous variable, participants will not be issued with a loan PAP therapy device. Participants will continue to use their usual PAP therapy device, with the introduction of the investigational product being the only intervention for the clinical investigation. This is unless the participant meets all inclusion and exclusion criteria, expect the exclusion criteria which specifies that the participant must use a PAP therapy device which possesses data recording capabilities to capture AHI and leak information that is accessible to

[redacted]. In such cases, the participant will receive a loaned a PAP therapy device with data recording capabilities from [redacted] if one is available, to use for the duration of the clinical investigation.

[redacted]

When leak is considered exceptionally high, the flow signal measured by devices can be disrupted, resulting in inaccurate residual AHI reporting. To counteract this, leak data will be analyzed on a nightly basis during both the baseline and intervention period. [redacted]

Leak Threshold	Justification
20 L/min	A study looked to characterize leak profiles to investigate a correlation between leak rate and clinical outcomes. The study used the 20 L/min threshold as a call for action from the sleep technologists to refit the mask during a polysomnography study, since measures above this flow rate interfered with polysomnographic signals.[18]
21 L/min	A study which investigated the effect of leak on ventilatory support and sleep architecture, found the 21 L/min flow rate to mark the threshold below which patients had improved oxygenation, decreased arousal index and an increase in rapid eye movement sleep.[19]
24 L/min	Published American Association of Sleep Medicine guideline parameters for successful unattended titration of APAP, deemed 24 L/min of mask leak as the acceptable amount of leak over 5 hours of treatment for APAP devices for treating adults with OSA.[20]

10.4. Testing Conditions

During this clinical investigation, fittings with the [redacted] and interviews with participants will be conducted at [redacted] no special conditions. Participants will use the [redacted] mask in place of their usual PAP therapy mask in a home environment or in settings where they sleep over the course of this clinical investigation.

10.5. Equipment

Aside from the investigational product and the associated components included within each packaged [redacted] bag issued to participants at [redacted] still and video camera, laptop, caliper, nasal depth measurement guide, and disinfectant cleaning wipes, will be necessary to carry out the activities detailed in this CIP. Participants will be expected to bring their usual mask and PAP therapy device to Visit 1 and Visit 2. All equipment will be shipped via courier from [redacted] before the clinical investigation commences. This equipment, in addition to a portion of clinical investigation documentation, will be [redacted] once the clinical investigation ends. The following equipment will be used during this clinical investigation.

Item	Quantity	Purpose
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

10.6. Participant Compensation

[redacted]

10.7. Informed Consent

F&P maintains a standard operating procedure for documenting the expected informed consent process, '*Obtaining Informed Consent*', which can be used if the investigation site does not maintain its own. A copy will be provided to the investigation site for review [redacted]

10.8. Case Report Form

This clinical investigation will utilize electronic CRFs [redacted] Only research personnel listed in the DOA are allowed to amend or make entries into the CRF.

10.9. Protocol Deviations

All deviations from the CIP shall be recorded together with an explanation. Deviations shall be reported to F&P in a timely manner and through the appropriate channels. [redacted] Where appropriate, deviations will be reported to the relevant IRB, competent authorities, or appropriate regulatory bodies. All deviations should be documented in the CRF for individual participants, or as a note to file to be included in the regulatory binder.

10.10. Event Timeline

[redacted]

[redacted]

Details of the key events that will occur during the clinical investigation are summarized below:

A. [redacted]

The follow will take place during recruitment:

[redacted]

[redacted].

Procedures that will be carried out at [redacted] are detailed below, and will be noted in the individual CRF for each participant:

[redacted]

[redacted]

C. [redacted]

D. [redacted]

E. [redacted]

F. [redacted]

G. [redacted]

H. [redacted]

Note that any steps marked with an asterisk (*) above are optional. Participants can opt into these activities, but they do not have to complete them necessarily to continue in the clinical investigation. If audio or video recording occurs, activities conducted in all steps will be recorded until reimbursement is issued. [redacted] Consenting activities planned to occur during recruitment may take place at Visit 1, depending on the availability of participants and ability to confirm enrolment eligibility due the first pre-screening phone call.

For the purpose of conducting fitting assessments with the [redacted] mask, the PAP therapy device used by participants will be adjusted to match the prescribed pressure setting, as per the following:

- For participants using APAP, this will be their average pressure for F&P devices, their median pressure if on a ResMed device, and their mean pressure if on a Philips Respironics device
- For participants using BPAP, this will be their IPAP
- For participants using CPAP, this will be their prescribed fixed pressure
- For participants where their usual pressure is unknown, the pressure will be set at a fixed pressure of 10 cmH_2O

10.11. Roles and Responsibilities

[redacted]

[redacted]

10.12. Withdrawal Criteria

Participants will be informed that they have the right to withdraw from the clinical investigation at any time, without prejudice or compromise to their medical care, and are not obliged to state their reasons. [redacted] Participants are informed that they can return to using their usual mask for PAP therapy during the clinical investigation if they have reason to do so. Withdrawal can occur in person at the investigation site, or by phone call or email. Upon withdrawal, the participant will be informed to immediately stop using the investigational product and to return all associated items and packaging to the investigation site at their earliest convenience. In the event of a participant being withdrawn during a scheduled or unscheduled visit at the investigation site, the investigational product will be retrieved from the participant. Thereafter, participants will no longer considered active in the clinical investigation. If the PI elects to withdraw a participant, the same procedure for investigational product reconciliation will be followed, and where serious or emergent medical attention is required, the PI will follow the usual emergency code of practice instituted at the investigation site.

The PI may withdraw a participant at any time for the following reasons:

- Protocol violation
- Safety concerns
- Serious illness
- AEs

Data from withdrawn participants may be used when results of the clinical investigation are analyzed if it is complete and accurate. If data from withdrawn participants is not used, [redacted] Participants will not be replaced after all original recruits have been attended their first appointment at the investigation site. If participants withdraw before this, another participant can be recruited as a replacement.

10.13. Follow-up Plan

All participants are free to receive standard care from their medical provider or healthcare professional throughout and after the completion of the clinical investigation. Participants will be followed up with throughout the duration of their enrolment in the clinical investigation, defined as the date informed consent is completed up to the date the participant either attends their final appointment at the investigation site or is formally withdrawn. [redacted], participants will be obliged to report any AEs or SAEs for 24 hours after either their last use of the investigational product or their last contact with the investigation site for the purposes of the clinical investigation, regardless of whether they have completed the clinical investigation or have been withdrawn. There will be no active follow-up during this period, but participants will be informed of the requirement to report any AEs appropriately. This 24-hour period is deemed acceptable because once the investigational product is no longer in contact with the participant, there is no mechanism for new AEs

related to the intervention to occur. Moreover, as the investigational product does not interact with internal systems or structures of the body and there are no metabolization risks or anticipated residual impacts on the individual. The most obvious risks associated with PAP therapy mask use which is incompatible with the user, such as reddening, itching, or swelling of the skin, generally appear quickly upon initial application of the medical device, but will subside when use is discontinued.

10.14. Foreseeable Complications

From the Manufacturer and User Facility Device Experience database, the common reported injuries from PAP therapy and associated interface use are pressure sores, leading to cuts, rashes, and skin abrasions and breakdown. Allergic reaction to materials in the interface can occur. Common complaints are discomfort and soreness on the areas of contact with the interface. Participants on the clinical investigation are informed that they can switch back to their usual mask if required. In instances of malfunction or damage, the investigational product and its components may be replaced, with this recorded in the CRF. In the event that participants require additional healthcare after they have been involved in this clinical investigation, and this medical attention is necessary because of the participant partook in the clinical investigation or differs from that normally expected as part of their usual healthcare or follow-up, the PI will be responsible for ensuring availability and access to appropriate healthcare. The investigation site will provide evidence of an emergency plan of action to F&P for any participants who required this additional healthcare.

[redacted]

11. Clinical Investigation Documentation

11.1. Case Report Form

Data from the clinical investigation will be recorded from source documents and transcribed to a CRF to enable the collection of participant data. [redacted]

11.2. Protocol Deviations

All deviations from the CIP shall be recorded in the CRF, with an explanation for the deviation, [redacted] Deviations shall be reported to F&P who is responsible for analyzing them and assessing their significance. The reasons for withdrawal and discontinuation of any participant from the investigation shall be recorded. If such discontinuation is related to the poor performance or safety of the investigational product, that participant will still be followed up with if possible. When and where relevant, ethics committees, competent authorities, or appropriate regulatory bodies will be informed about protocol deviations and protocol violations.

12. Statistical Considerations

12.1. Description of Statistical Design

The statistical design of this clinical investigation is aimed at evaluating the product requirements as defined by the respective [redacted] mask is safe and effective prior to its release into global markets and to support regulatory clearance applications where required. Therefore, the statistical design of this clinical investigation is considerate of its objectives and endpoints being confirmatory in nature, rather than exploratory, or in the pilot stage. [redacted]

Data from participant questionnaires and compliance reports will be saved in supporting folders of the [redacted] For each participant and requirement, it will be determined if these have been met individually based on the acceptance criteria. Minitab will be used to perform a one-sided one-proportion test on each requirement using the corresponding confidence limit to confirm that the acceptance criteria has been met.

Details are as follows:

- H_0: Proportion = Reliability Limit
- H_1: Proportion > Reliability Limit
- Acceptance criteria: $P \leq 0.05$ to reject H_0

12.2. Pass and Fail Criteria

Below are the acceptance criteria for the product validation aspect of this clinical investigation, used to evaluate aspects of the investigational product, and that may be used as evidence to further develop areas where a poor result is observed. Any requirements relating to marketing claims are for observational purposes only, so will not have acceptance criteria. A summary of this information is provided in the corresponding [redacted]

[redacted]

[redacted]

12.3. Statistical Termination and Procedure Deviations

No interim analysis will be conducted as statistical outcomes will not change the conduct of the clinical investigation. Statistical procedure deviations will be reported to the PI and the sponsor. Deviations from the original statistical plan will be explained in the final study report, located in [redacted]

12.4. Selection Criteria

Data from all participants who use the investigational product as part of this clinical investigation will be included in the analysis, unless a clear reason for exclusion is present, such as definitive proof the participant was not using the investigational product during the intervention period. Any data points that are excluded will be documented clearly with the reason for their exclusion. For participants who have withdrawn, all data collected up to the point of withdrawal may be used in the analysis, provided the data is complete and accurate.

12.5. Statistical Data Management

F&P may consult an external statistician to assist with the analysis of the data collected from participants.

13. Safety and Reporting

13.1. Emergency Contact Details

Name	[redacted]
Institution	[redacted]
Designation	[redacted]
Address	[redacted]
Phone	[redacted]
Email	[redacted]

Name	[redacted]
Institution	F&P
Designation	[redacted]
Address	15 Maurice Paykel Place East Tamaki Auckland, 2013 NZ
Phone	[redacted]
Email	[redacted]
Residence	NZ
Responsibilities	Ensuring quality management processes and procedures are followed, carrying out the monitoring plan, assisting with provision of investigational product, documenting significant protocol exemptions, as well as selecting and training research personnel.

Adverse events (AE) and serious adverse events (SAE) will be captured as part of the clinical investigation in the CRF of the affected participant and on a Serious Adverse Event Form (SAEF). There will be no greater risk to participants if they partake in the clinical investigation as [redacted] will be following routine practice for the medical supervision of those using PAP therapy to manage respiratory conditions. Participants in the clinical investigation may benefit from receiving advice regarding PAP therapy or the respiratory condition for which they are using the treatment, as well as regular medical follow-up.

13.2. Non-significant Risk

F&P has assessed the potential risk of the investigational product when used as part of this clinical investigation, and believe it to be a non-significant risk. This clinical investigation will attempt to recruit individuals who have already been prescribed and are currently undergoing in-home PAP therapy as treatment for a respiratory condition. [redacted]

13.3. Adverse Events

An AE is any adverse change from the baseline condition of a participant, and is considered as any unfavorable and unintended symptom or disease that occurs over the course of the clinical investigation, whether related or unrelated to use of the investigational product or PAP therapy. All clinically significant AEs that occur during the clinical investigation that were not present prior to commencement of the clinical investigation, will be recorded in the CRF of the affected participant, and followed up by the PI until resolution or stabilization of the condition among participants occurs in accordance with GCP. The collection of AE data will commence once the participant is fitted with the investigational product at Visit [redacted] and up to 24 hours after the investigational product is returned at [redacted]

13.4. Serious Adverse Events and Reporting

SAEs are considered any harmful outcomes experienced by participants which result in any of the following, regardless of their relationship to use of the investigational product or PAP therapy:

- Death
- Life-threatening AE
- Unplanned in-patient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability or incapacity
- Permanent irreversible impairment of a body function or damage to a body structure
- Congenital abnormality or birth defect

[redacted]

13.5. Expected Side Effects

Throughout the clinical investigation, participants may experience a poor night sleep with the investigational product as it will be different to the usual mask they use. These are disclosed in the ICF issued to participants and will be documented as expected side effects in the CRF, but not as AEs. Participants will be informed that these side effects are expected as a consequence of receiving PAP therapy, particularly when you initially begin use, and may subside over time with continued adherence to treatment. They will also be advised that if these side effects are unduly intrusive to their daily life or prevent them from using PAP therapy to manage the respiratory condition for which it was prescribed, to consult the PI or contact the investigation site. Alternatively, participants can switch back to using their usual mask for PAP therapy.

13.6. Early Termination

The clinical investigation may be discontinued at any time on advice or instruction from the PI, or on the basis of new information regarding the safety or efficacy of the investigational product arising. Moreover, the clinical investigation may be terminated if progress is unsatisfactory.

The following is required if the appropriate party decides to terminate the clinical investigation:

- If the PI terminates or suspends the clinical investigation without prior agreement with F&P, the PI should inform the institution, when and where required by the applicable regulatory requirements. The PI and institution should promptly inform F&P and the IRB, and provide a detailed written explanation of the termination or suspension
- If F&P terminates or suspends the clinical investigation, the PI should promptly inform the institution, when and where required by the applicable regulatory requirements. The PI and institution should promptly inform the IRB, and provide a detailed written explanation of the termination or suspension
- If the IRB terminates or suspends its approval or favorable opinion of the clinical investigation, the PI should inform the institution, when and where required by the applicable regulatory requirements. The PI and institution should promptly inform F&P, and provide a detailed written explanation of the termination or suspension.

14. Publication Policy

14.1. Presenting Results

[redacted]

15. Approval

15.1. Principal Investigator and Sponsor Signatures

All the required signatories for the approval of this document by F&P are listed on the second page of this CIP alongside their relevant positions. Signing the below approval indicates that the PI and F&P agree to this version of CIP.

[redacted]

16. Regulatory and Document Sources

16.1. Internal References

[redacted]	[redacted]
[redacted]	[redacted]
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[redacted]	[redacted]
[redacted]	[redacted]

16.2. External References

[redacted]

17. References

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18. Appendices

18.1. [redacted]

[redacted]

[redacted]

18.2. [redacted]

18.3. [redacted]

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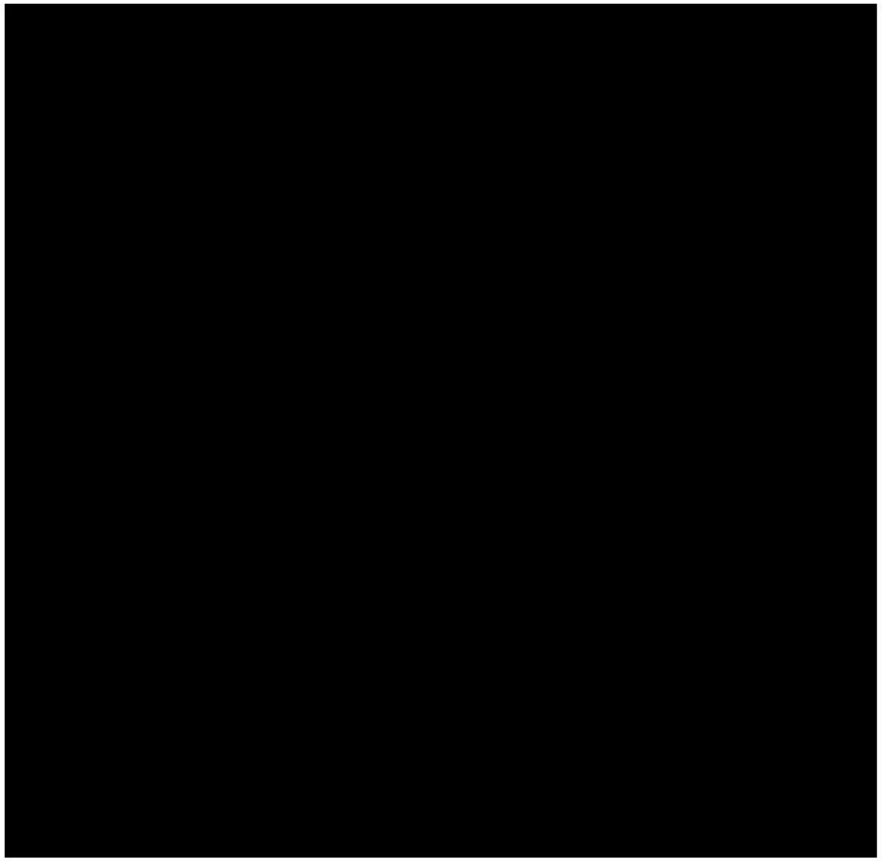

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