A Development Study to Evaluate a Nasal Mask for the Treatment of Obstructive Sleep Apnea

NCT04011826

DATE: 17 October 2019

Fisher & Paykel HEALTHCARE

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Clinical Investigation Plan

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1. Revision History

Revision	[redacted]	Date	[redacted]
A		11 June 2019	
B		10 July 2019	
C		17 October 2019	

1.1. List of Abbreviations

AE	Adverse Event
AHI	Apnea Hypopnea Index
APAP	Automatic Positive Airway Pressure
BPAP	Bi-Level Positive Airway Pressure
CIA	Clinical Investigation Administration
CIP	Clinical Investigation Plan
CPAP	Continuous Positive Airway Pressure
CRF	Case Report Form
CSI	Clayton Sleep Institute
F&P	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

[redacted]

OSA	Obstructive Sleep Apnea
PAP	Positive Airway Pressure
SAE	Serious Adverse Event
SME	Subject Matter Expert
UI	User Instructions

2. Document Information

2.1. Purpose and Scope

The purpose of the trial is to evaluate the performance, comfort and ease of use (usability) of the F&P Nasal mask in the home environment in regards to satisfaction.

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

F&P will be conducting the study, and as such the investigators will monitor the progress of the investigation. Planned monitoring activities will take place at Visit 1, 2 and 3 by a F&P Clinical Researcher as well as once during the course of the study extension as outlined below:

[redacted]

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, 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 Fisher & Paykel Healthcare. Original Informed Consent Forms and copies of the CRF will be stored on site at Clayton Sleep Institute (CSI) for 15 years.

3. Investigator Information

3.1. Principal Investigator

Name: Mark Muehlbach

Address: 2531 S Big Bend Blvd, Maplewood, MO 63143, USA

Phone: 314-645-5855

Professional Position: Clinical Director

3.2. Coordinating Investigator

Name: Mr. Matthew Lee Uhles

Address: 2531 S Big Bend Blvd, Maplewood, MO 63143, USA

Email: uhlesm@claytonsleep.com

Phone: 314-645-5855 Ext 318

Professional Position: Chief Operating Officer

[redacted]

3.3.

[redacted]

3.4. Institution

Name: Clayton Sleep Institute

Address: 2531 S Big Bend Blvd, Maplewood, MO 63143, USA

Email: uhlesm@claytonsleep.com

Phone: 314-645-5855

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: Bhavi Ogra

Phone: +64 9 574 0123 Ext 7882

Email: bhavi.ogra@fphcare.co.nz

Profession: Clinical Research Manager

Country of residence: New Zealand

[redacted]

[redacted]

[redacted]

5. Device Information

5.1. Identification of the Medical Device

The F&P Nasal is a nasal mask which is primarily used in combination with a Positive Airway Pressure (PAP) therapy device to administer PAP therapy either in a patient's home or in the hospital.

[redacted]

5.2. Device Risk Analysis and Management

The acceptability of the risk associated with the device is derived from the benefit associated with positive airway pressure (PAP) therapy via a nasal mask for patients with OSA, and the generally accepted state of the art (currently and generally accepted as standard. CPAP flow generators, PAP therapy masks and info technology share the same risk acceptability criteria because they all provide the same overall benefit and the general accepted state of the art is close enough for the criteria to be shared.

The primary benefit of PAP therapy is the treatment of OSA to reduce disease severity (as measured by the AHI) and improve daytime sleepiness and fatigue. Good evidence has accumulated that effective CPAP improves the neurobehavioral and cardiovascular consequences of OSA[1,2]. PAP therapy is the gold standard treatment for OSA and the benefits of treatment have been clearly shown to outweigh any risks of treatment in the OSA population [redacted].

[redacted]

[redacted]

[redacted]

6. Justification for a Clinical Trial

6.1. Synopsis

The investigation is a prospective, non-randomized, non-blinded study. This investigation is designed to evaluate the performance (leak and comfort) as well as participant's overall acceptance of the F&P Nasal mask amongst participants with diagnosed OSA. A minimum of 45 participants with OSA currently using a nasal, sub-nasal and/or pillows mask will be recruited by CSI. The phone recruitment script is available in Appendix A. CSI will recruit all participants within three weeks of beginning of the study.

This study will involve a baseline visit (Visit 1) where participants' informed consent for the F&P Nasal mask trial (CIA-262) will be gained. The participant's prescribed PAP therapy treatment settings will be gathered as well. Participants will also fill out a questionnaire (Appendix B) to gain a better understanding of their satisfaction of their current mask.

Visit 2 will take place 7 ± 3 days after Visit 1. At this visit, participants will be fitted with the F&P Nasal mask and will be asked a few questions in the form of a structured questionnaire. Initial impressions, comments and photographs will be captured via recorded audio and video (provided the participant has given consent). If the participant does not provide video and/or audio consent, only written notes will be taken. Baseline efficacy data will be downloaded from participants' PAP/BPAP therapy devices. Participants will also be issued a sleep diary (Appendix C) to record daily feedback of the Nasal mask.

A follow up phone call will be made by CSI 3±1 days after Visit 2 and feedback will be recorded in the CRF.

Visit 3 will take place 14 ± 3 days after Visit 2. The participants will return to the site and provide their feedback on the F&P Nasal mask in the form of verbal comments and a structured questionnaire (Appendix B and D). Photographs will be captured as well as audio and video will be recorded during this visit (provided the participant has given consent). If the participant does not provide audio and/or video consent, only written notes will be taken. F&P Nasal efficacy data will be downloaded from participants' PAP/BPAP therapy devices. If the participant prefers their usual mask over the F&P Nasal mask, they will return the F&P Nasal mask and the User Instruction (UI) and return to using their usual mask and will be considered to have completed the investigation.

If the participants prefer the F&P Nasal mask to their usual mask they will be invited to continue to use the F&P Nasal mask in-home for an additional 6 months. Monthly phone calls will be made and recorded in the CRF and at the end of six months the participants will be asked to return the mask and UI to CSI and provide their feedback in the form of verbal comments and a structured questionnaire (Appendix B). This will mark the 4th Visit and end of the extension part of the trial. Participants will return the F&P Nasal mask, and continue using their usual mask.

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 ranging from 9% to 38% in the general adult population[3] 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 (BPAP). Despite the effectiveness of PAP in abolishing upper airway obstruction, acceptance of and adherence with therapy has been sub-optimal[4,5]. 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[6,7].

[redacted]

6.5. Justification for Administration

Participants will remain on their prescribed PAP /BPAP therapy pressures and devices during the duration of the trial. Baseline PAP /BPAP therapy data on the participant's usual mask will be collected after 7 ± 3 days in order to evaluate treatment efficacy compared to the investigational mask. Participants will not be randomised to use the F&P Nasal in-home for 14 ± 3 days.

7. Objectives of the Clinical Investigation

7.1. Hypothesis

[redacted]

7.2. Objectives

Primary Objective:

- To evaluate the performance, comfort and ease of use (usability) of the F&P Nasal mask in a home environment in regards to the participants' view on overall comfort, overall experience and satisfaction.

Secondary Objective:

- To evaluate the performance, comfort and ease of use (usability) of the F&P Nasal mask in a home environment in regards to the participants' view on overall comfort, overall experience and satisfaction over time.

7.3. Population

This investigation is a prospective, randomized, non-blinded study. This investigation is designed to evaluate the performance, comfort and ease of use of the F&P Nasal mask amongst a minimum of 45 participants diagnosed with OSA who are current nasal, sub-nasal or pillows users.

[redacted]

[redacted]

7.6. Type of Investigation

This is an open-label (investigators and participants are non-blinded and informed of intended treatment device) single arm study. The F&P Nasal will provide effective treatment similar to the

[redacted]

participant's usual CPAP mask. The intended treatment F&P Nasal will not be randomized – as the intention is not to compare between masks therapies.

7.7. Controls

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

7.8. 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.

7.9. End Points

7.9.1. Primary Outcome

- The F&P Nasal mask provides adequate therapy for OSA during in-home use.

7.9.2. Secondary Outcomes

- The F&P Nasal mask is rated easy to use by the participant.
- The F&P Nasal mask is rated as comfortable to use by the participant.
- The F&P Nasal mask is rated overall by the participant as satisfactory.

7.10. 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 mask through a custom designed ease of use usability script
General Demographics	To gather participants general demographics
Preference	To assess which mask

[redacted]

	the participants prefers to use going forward.
Mask performance	To assess the mask's performance in relation to leak

[redacted]

[redacted]

[redacted]

7.12. Equipment

Participants will use their own PAP/BPAP therapy devices with their prescribed pressures.

[redacted]

7.13. Inclusion / Exclusion criteria

Inclusion Criteria

- Diagnosis of OSA by Physician
- ≥ 22 years of age
- ≥ 66 lbs
- Prescribed PAP or BPAP therapy for OSA
- Existing nasal, sub-nasal and pillows mask users for approximately three months prior to enrollment in this investigation
- Fluent in written and spoken English

Exclusion Criteria

- Inability to give informed consent
- Pregnant or think they may be pregnant
- PAP Intolerant
- Anatomical or Physiological Conditions that make PAP therapy inappropriate

- Participant's PAP/Bi-level device without efficacy data recording capabilities
- IPAP pressure of >25cmH20
- PAP/BPAP therapy device usage for delivery of medicines with exception of oxygen

7.14. Point of Enrolment

Participants will be recruited from patients who are prescribed either APAP, CPAP or BPAP devices for OSA therapy at Clayton Sleep Institute. The principal investigator (or those identified in delegation log) will ask the subjects whether they're interested to take part in the trial. The participants who provide informed consent and meet the inclusion/exclusion criteria will then be enrolled into the trial.

7.15. 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.

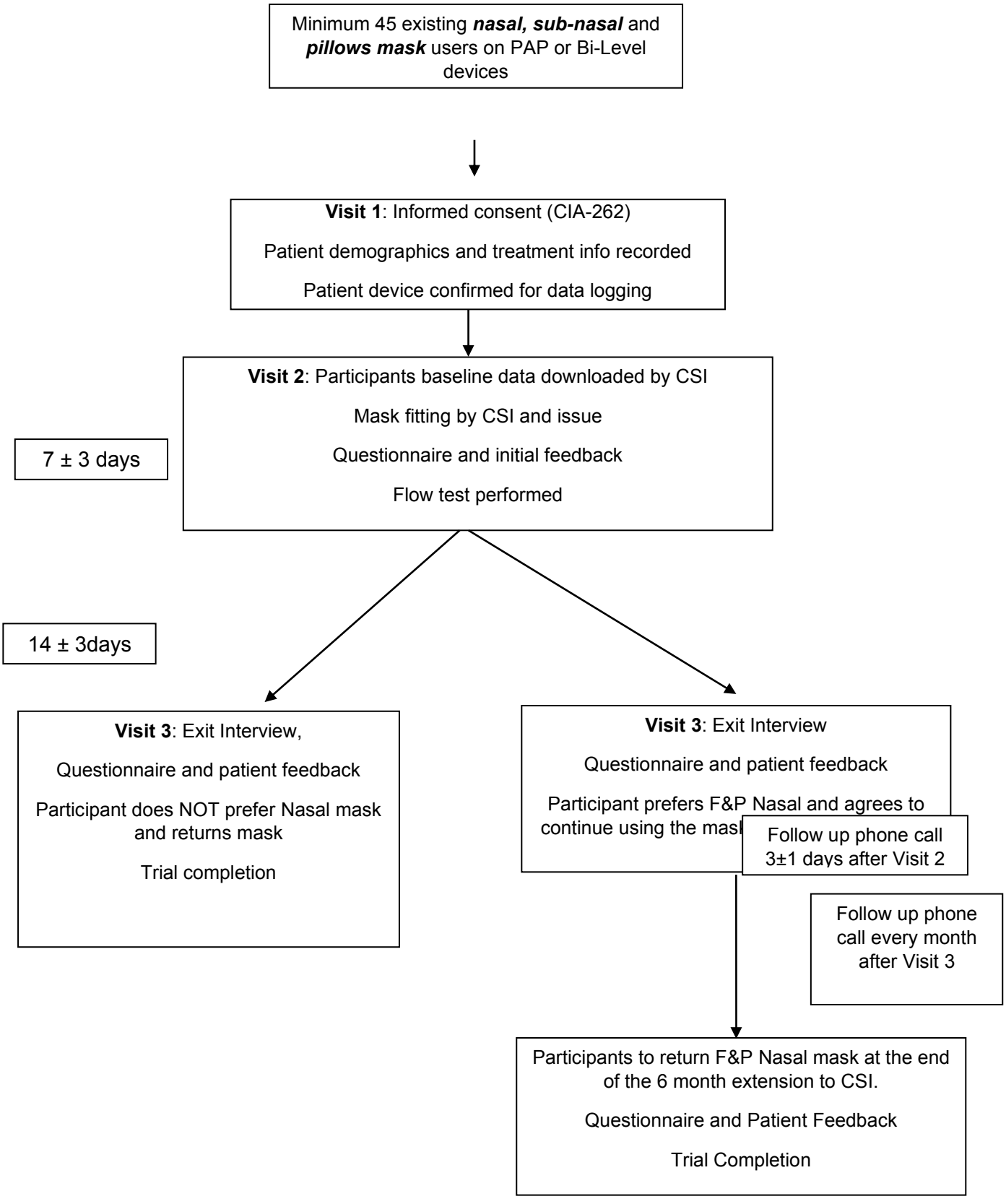
EVENTS	Visit One	Visit Two	Phone Call	Visit Three	Phone call	Phone call	Phone call	Phone call	Phone call	Visit Four
Informed consent (CIA-262)	**X**									
Commence baseline data gathering	**X**									
Participant Questionnaire (see Appendix B)	**X**	**X**								
Mask fitting with F&P Nasal mask		**X**								
Static Leak Measurement		**X**								
Issue complete Nasal mask with UI		**X**								
Sleep Diary Issued		**X**								
Researcher Questionnaire (see Appendix C)		**X**		**X**						
Baseline PAP device data downloaded		**X**								
Commence in-home trial of the F&P		**X**								

[redacted]

EVENTS	Visit One	Visit Two	Phone Call	Visit Three	Phone call	Phone call	Phone call	Phone call	Phone call	Visit Four
Nasal mask										
Phone call			X							
Return the F&P Nasal mask				X						
PAP device data downloaded		X		X						
AE/SAE assessment		X	X	X	X	X	X	X	X	X
Commence F&P Nasal extension if participant agrees				X						
Phone call (extension month 1)					X					
Phone call (extension month 2)						X				
Phone call (extension month 3)							X			
Phone call (extension month 4)								X		
Phone call (extension month 5)									X	
PAP device data downloaded										X
Return F&P Nasal mask.										X
Participant Questionnaire (see Appendix B)										X

[redacted]

[redacted]


Minimum 45 existing ***nasal, sub-nasal*** and ***pillows mask*** users on PAP or Bi-Level devices
Visit 1: Informed consent (CIA-262)
Patient demographics and treatment info recorded
Patient device confirmed for data logging
Visit 2: Participants baseline data downloaded by CSI
Mask fitting by CSI and issue
Questionnaire and initial feedback
Flow test performed
7 ± 3 days
14 ± 3days
Visit 3: Exit Interview,
Questionnaire and patient feedback
Participant does NOT prefer Nasal mask and returns mask
Trial completion
Visit 3: Exit Interview
Questionnaire and patient feedback
Participant prefers F&P Nasal and agrees to continue using the mas
Follow up phone call 3±1 days after Visit 2
Follow up phone call every month after Visit 3
Participants to return F&P Nasal mask at the end of the 6 month extension to CSI.
Questionnaire and Patient Feedback
Trial Completion

[redacted]

[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]

7.16. 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 participant at any time for the following reasons:

- 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.

7.17. Number of Trial Subjects

A minimum of 45 nasal, sub-nasal and pillows mask users for OSA therapy will be recruited into this trial.

7.18. Follow up Plan

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

[redacted]

[redacted]

STATISTICAL CONSIDERATIONS

7.20. 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.

[redacted]

[redacted]

7.22. Statistical Termination

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

7.23. 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.

[redacted]

7.25. Statistical Data Management

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

8. 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 AE's occurring during the study will be assessed at each subsequent visit and phone call to assess any change to the subject's health status since the previous interaction. Any change in health status will be recorded on CRF and evaluated by the PI.

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]

[redacted]

8.3. 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.

8.4. 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.

8.4.1. 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.

8.4.2. 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.

8.4.3. Institutional Review Board (IRB) or Independent Ethics Committee (IEC)

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.

9. 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.

10. 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. Signing the below approval indicates that the primary investigator (PI) agrees to this version of CIP.

[redacted]

11. References

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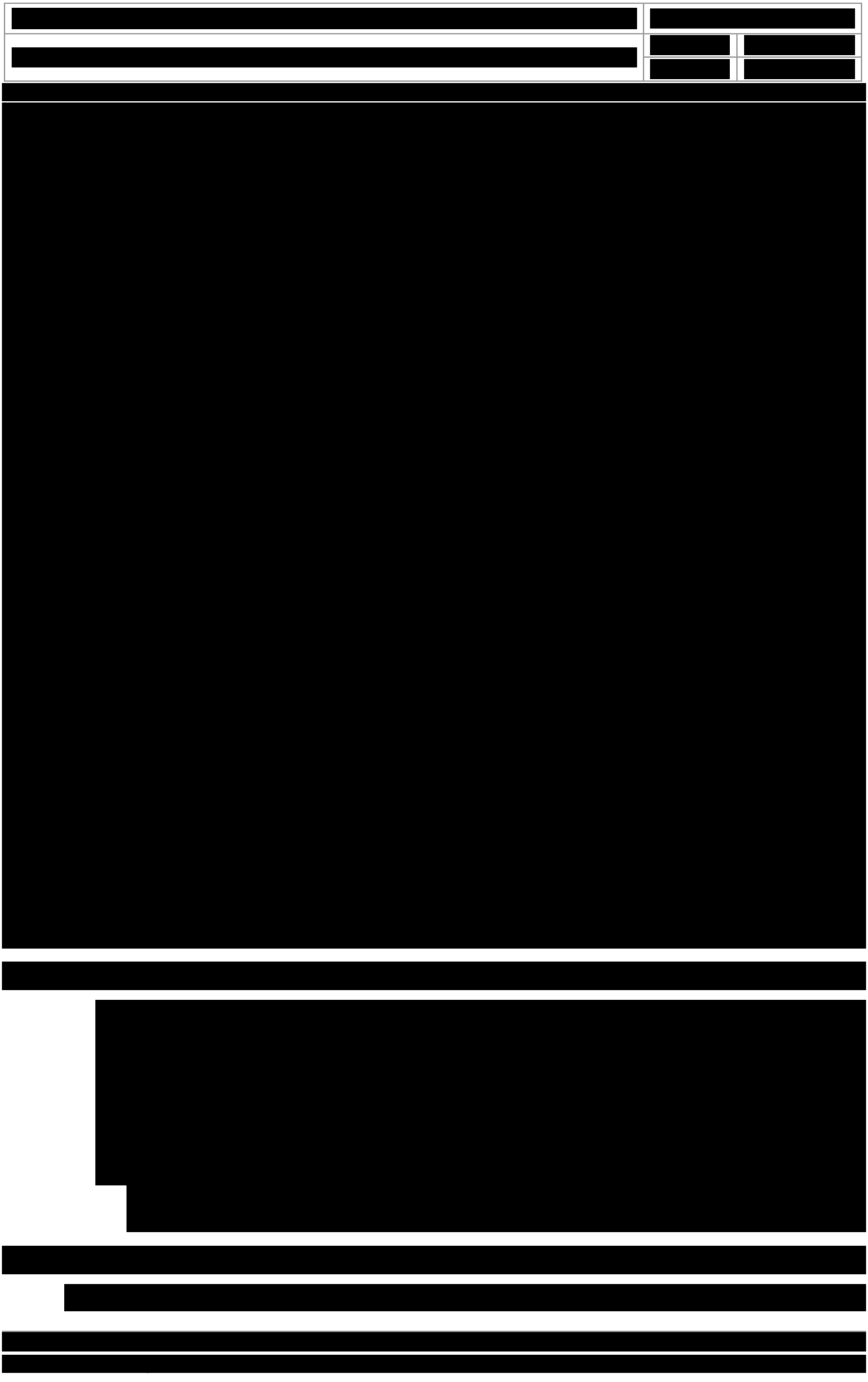

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