Official Title: A pivotal, prospective, multi-center, open-label study evaluating the safety and effectiveness of the Cochlear™ Osia® 2 System in a pediatric population

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Clinical Investigation Plan

Investigation Title: A pivotal, prospective, multi-center, open-label study evaluating the safety and effectiveness of the Cochlear™ Osia® 2 System in a pediatric population.

Short Title:	**Osia Peds Expansion**
CIP Number:	**CAM5766**
Version and Date:	**Refer to system version control**
Sponsor:	**Cochlear Americas** **10350 Park Meadows Drive** **Lone Tree, Colorado, USA 80124**

This clinical investigation shall be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, International Standard ISO 14155:2020 Clinical investigation of medical devices for human subjects - Good Clinical Practice, 21 CFR Parts 812, 56, 54, 50 & 11 as well as any regional or national regulations, as applicable.

Manufacturer	Cochlear Limited 1 University Avenue Macquarie University, NSW2109
Sponsor Organisation(s)	Cochlear Americas 10350 Park Meadows Drive Lone Tree, Colorado USA 80124
Funding Source	Sponsoring Organisation(s)
Contract Services Statistician	NAMSA Minneapolis - St. Louis Park 400 Highway 169 South, Suite 500 Minneapolis, Minnesota 55426 United States
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A complete list of participating Principal Investigators' names, titles and addresses, and the names and addresses of participating institutions (sites) will be maintained by the Sponsor and will be provided as a separate Principal Investigator List. The definitive Principal Investigator list will be provided in the Clinical Investigation Report.

INVESTIGATOR AGREEMENT

Investigator Declaration

By my signature below, I confirm that I have read, understood and will strictly adhere to the requirements therein. I undertake to ensure that all staff with delegated responsibilities in the conduct of this CIP have also read, understood and will strictly adhere to the requirements therein. This CIP will not be implemented without prior written approval from the Ethics Committee, any applicable National Competent Authorities, and the Sponsor. If amendments to this plan become necessary, written approval by the Ethics Committee and any applicable National Competent Authorities will be obtained before the changes are clinically implemented per the amendment, except under emergency circumstances to protect the rights, safety, and well-being of subjects.

I also agree that my personal information may be provided to regulatory agencies and public clinical trial registry platforms and stored in their systems in order to comply with regulatory requirements. Examples of the type of personal information include my name, signature and summary of qualifications.

Name	**Title**
	Principal Investigator
Site Name	**Site Address**
Signature	**Date**

TABLE OF CONTENTS

Definitions and Abbreviations 7
1 Clinical Investigation Synopsis 9
2 Schedule of Events 12
3 Background Information and Rationale 15
3.1 Introduction 15
3.2 Findings of Previous Nonclinical and Clinical Studies 15
3.2.1 Nonclinical Data 15
3.2.2 Clinical Data 15
3.3 Study Rationale 17
4 Medical Device Information 17
4.1 Identity and Description of the Investigational Medical Device (IMD) 17
4.2 Identity and Description of the Comparator 18
4.3 Accessory Device Requirements 18
5 Objectives 18
5.1 Primary Objective 18
5.2 Secondary Objective 18
5.3 Exploratory Objective 18
6 Design of the Clinical Investigation 19
6.1 General 19
6.1.1 Design Rationale 19
6.2 Subjects 20
6.2.1 Inclusion Criteria 20
6.2.2 Exclusion Criteria 20
6.2.3 Number of Subjects Required 21
6.2.4 Vulnerable Populations 21
6.2.5 Recruitment and Study Duration 22
6.2.6 Criteria and Procedures for Subject Withdrawal 23
6.2.7 Randomisation Procedures 23
6.2.8 Post-investigation Medical Care 23
6.3 Evaluations and Procedures 23
6.3.1 Screening/eligibility 24
6.3.2 Performance/Effectiveness 24
6.3.3 Safety Evaluations and Procedures 26
6.3.4 Detailed Visit Schedule 26
6.4 Equipment Used for Evaluations and Procedures 28

6.5 Sponsor Role in Conduct of the Clinical Investigation 28
7 Benefits and Risks of the Investigational medical device and Clinical Investigation 29
7.1 Anticipated Clinical Benefits 29
7.2 Anticipated Adverse Device Effects 29
7.2.1 Risks Associated with the Surgery 29
7.2.2 Risks Associated with Implantation of the Study Device 29
7.2.3 Risks Associated with Use of the Study Device 30
7.2.4 Risks Associated with Simultaneous Aural Atresia and Microtia Repair 30
7.3 Risks Associated with Participation in the Clinical Investigation 31
7.4 Risk Mitigation 31
7.5 Benefit-to Risk Rationale 31
8 Statistical Considerations 32
8.1 General Considerations 32
8.2 Endpoints 32
8.2.1 Primary Endpoint 32
8.2.2 Secondary Endpoints 32
8.2.3 Exploratory Endpoints 32
8.3 Hypotheses 33
8.3.1 Primary Hypothesis 33
8.3.2 Secondary Hypotheses 33
8.3.3 Exploratory Hypothesis 34
8.4 Sample Size Determination 34
8.5 Analysis Populations 34
8.6 Endpoint Analyses 35
8.6.1 Primary Endpoint Analyses 35
8.6.2 Secondary Endpoint Analyses 35
8.6.3 Exploratory Endpoint Analyses 35
8.7 Safety Analyses 35
8.8 Interim Analyses 35
9 Informed Consent Process 35
10 Adverse Events and Device Deficiencies 36
10.1 Definitions 36
10.1.1 Adverse Event 36
10.1.2 Adverse Device Effect 36
10.1.3 Serious Adverse Event 36
10.1.4 Serious Adverse Device Effect 37

10.1.5 Unanticipated Serious Adverse Device Effect 37
10.1.6 Adverse Events of Special Interest 37
10.1.7 Device Deficiency 37
10.1.8 Serious Health Threat 37
10.2 Recording and Handling of Adverse Events 38
10.2.1 Assessment of Severity 38
10.2.2 Assessment of Causality 38
10.2.3 Assessment of Seriousness 40
10.2.4 Assessment of Expectedness 40
10.2.5 Non-reportable Adverse Events 40
10.3 Recording and Handling of Device Deficiencies 40
10.4 Reporting Responsibilities 40
10.4.1 Investigator Reporting of Serious Adverse Events 41
10.4.2 Sponsor Notification of Events 41
10.5 Independent Data Monitoring Committee 41
11 Device Accountability 41
12 Deviations from the Clinical Investigation Plan 42
13 Data Management 43
13.1 Source Data 43
13.2 Methods for Data Entry and Collection 43
13.3 Database Lock 43
14 Confidentiality 44
15 Ethics Committee and Regulatory Authority Approval 44
16 Suspension or Premature Termination 44
17 Amendments to the Clinical Investigation Plan 45
18 Record Keeping and Retention 45
19 Publication Policy 45
20 Statements of compliance 46
21 Quality Control and Assurance 46
21.1 Monitoring 46
21.2 Audits 47
22 Trademarks and Copyright 47
23 References 47
24 Change History. 48
Appendices 49
Appendix 1: Statement/Declaration of Device Conformity 49

DEFINITIONS AND ABBREVIATIONS

Term	Description
AC	Air Conduction
ADE	Adverse Device Effect
AE	Adverse Event
BC	Bone Conduction
CBAS	Cochlear Bone Anchored Solutions AB
CER	Clinical Evaluation Report
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CRF	Case Report Form
CRO	Contract Research Organization
CROS	Contralateral Routing of Signals
DD	Device Deficiency
EC	Ethics Committee Synonymous abbreviations/terms include: IRB (Institutional Review Board) IEC (Institutional Ethics Committee or Independent Ethics Committee) HREC (Human Research Ethics Committee)
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
FS	Fitting Software
GCP	Good Clinical Practices
IB	Investigator's Brochure
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
IFU	Instructions for Use
IMD	Investigational Medical Device
IOTS	Intraoperative Test System
ISO	International Organization for Standardization
OFS	Osia Fitting Software
PI	Principal Investigator

Term	Description
PIL	Principal Investigator List
PTA	Pure Tone Average
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOP	Standard Operating Procedure
SNHL	Sensorineural Hearing Loss
SNR	Signal to Noise Ratio
SP	Sound Processor
SSD	Single-Sided Deafness
SSQ	Speech, Spatial, and Qualities Hearing Scale
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

1 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A pivotal, prospective, multi-center, open-label study evaluating the safety and effectiveness of the Cochlear™ Osia® 2 System in a pediatric population.
Short title	Osia Peds Expansion
Investigation number	CAM5766
Name of investigational medical device(s)	Osia 2 System
Intended use of investigational medical device(s)	The Investigational Medical Device (IMD) is cleared for the following intended use: transmit sound to the cochlea (inner ear) via bone conduction with the purpose of enhancing hearing. Current indications for use: • Patients 12 years of age or older. • Patients who have a conductive or mixed hearing loss and still can benefit from sound amplification. The pure tone average (PTA) bone conduction (BC) threshold (measured at 0.5, 1, 2, and 3 kHz) should be better than or equal to 55 dB HL. • Bilateral fitting of the Osia System is intended for patients having a symmetrically conductive or mixed hearing loss. The difference between the left and right sides' BC thresholds should be less than 10 dB on average measured at 0.5, 1, 2, and 3 kHz, or less than 15 dB at individual frequencies. • Patients who have profound sensorineural hearing loss in one ear and normal hearing in the opposite ear (i.e., single-sided deafness or "SSD"). The pure tone average air conduction hearing thresholds of the hearing ear should be better than or equal to 20 dB HL (measured at 0.5, 1, 2, and 3 kHz). • The Osia System for SSD is also indicated for any patient who is indicated for an air-conduction contralateral routing of signals (AC CROS) hearing aid, but who for some reason cannot or will not use an AC CROS. • Prior to receiving the device, it is recommended that an individual have experience with appropriately fitted air conduction or bone conduction hearing aids. Current contraindications for use: • Insufficient bone quality or quantity to support implantation of both the BI300 Implant and the [OSI Implant Series] • Chronic or non-revisable vestibular or balance disorders that could prevent benefit from the device, as determined by good clinical judgement • Abnormally progressive hearing loss • Evidence that hearing loss is bilateral retro cochlear or bilateral central origin • Evidence of conditions that would prevent good speech recognition potential as determined by good clinical judgment • Skin or scalp conditions that may preclude attachment of the Audio Processor or that may interfere with the use of the Audio Processor

Name and description of comparator device/product(s)	Not applicable
Estimated recruitment period	12 months
Expected duration per subject	14-18 months
Number of subjects planned	50 subjects
Number of investigational sites planned	Up to 10 sites
Inclusion criteria	• Individuals aged 5 to 11 years of age with the following criterion: A conductive or mixed hearing loss and still can benefit from sound amplification. The pure tone average (PTA) bone conduction (BC) threshold (measured at 0.5, 1, 2, and 3 kHz) should be better than or equal to 55 dB HL. Note: Candidates include individuals seeking new implantation unilaterally (in one ear) or individuals already implanted with a bone-anchored device seeking a second-side implant (sequential bilateral). OR A profound sensorineural hearing loss in one ear and normal hearing in the opposite ear (i.e., single-sided deafness or "SSD"). The pure tone average air conduction (AC) hearing thresholds of the hearing ear should be better than or equal to 20 dB HL (measured at 0.5, 1, 2, and 3 kHz). • Prior experience with amplified sound through properly fitted amplification device such as a hearing aid, a CROS device, or a bone conduction device on a softband or sound arc. • Parent or Legal Guardian who is willing and able to provide written informed consent for the study participant.
Exclusion criteria	• Insufficient bone quality or quantity to support implantation of both the BI300 Implant and the OSI200 Implant. • Chronic or non-revisable vestibular or balance disorders that could prevent benefit from the device, as determined by the investigator. • Abnormally progressive hearing loss. • Evidence that hearing loss is bilateral retro cochlear or bilateral central origin. • Evidence of conditions that would prevent good speech recognition potential as determined by the investigator. • Skin or scalp conditions that may preclude attachment of the Sound Processor or that may interfere with the use of the Sound Processor. • Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator. • Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.

	• Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of this investigation. • Currently participating, or participated within the last 30 days, in another clinical investigation involving an investigational • Individuals undergoing simultaneous single-stage aural atresia or microtia repair due to the increased risk of skin complications associated with ear reconstruction.

Primary objective(s)	To demonstrate the safety of the Osia 2 System in a pediatric population aged 5 – 11 years by quantifying the type, frequency and severity of adverse events.
Secondary objective(s)	• To compare preoperative performance compared to postoperative performance in parental questionnaires using the Osia 2 System. • To compare preoperative unaided bone conduction thresholds to postoperative unaided bone conduction thresholds. • To compare unaided preoperative speech perception performance in quiet to aided speech perception performance postoperatively using the Osia 2 System. • To compare unaided preoperative adaptive speech in noise performance to aided adaptive speech in noise performance using the Osia 2 System.
Primary endpoint(s)	To quantify the type, frequency and severity of adverse events and serious adverse events Surgery through Visit 4 6 Months post-surgery.
Secondary endpoint(s)	• Mean difference between preoperative Baseline performance on the Speech Spatial & Qualities of Hearing Questionnaire (SSQ) – Parent version to Visit 4 6 Months post-surgery • Mean difference in individual subject PTA 500, 1, 2, and 4kHz Baseline to Visit 2 4 weeks post-surgery. • Mean difference between Baseline unaided speech perception in quiet and the aided condition using the Osia 2 system at Visit 4 6 Months post-surgery on open-set monosyllabic word recognition (CNC Words) in quiet. • Mean difference between baseline unaided speech perception in noise and the aided condition using the Osia 2 system at Visit 4 6 Months post-surgery on an adaptive speech in noise test (BKB SIN).

2 SCHEDULE OF EVENTS

Visit Type	Screening	Baseline	Surgery	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Timing of Investigation	**Day -60**	**Day -60**	**Day -0**	**Week 2**	**Week 4**	**Month 3**	**Month 6**	**Month 12**
Visit window (±) (calendar days)	NA	NA	NA	**± 7 Day**	**± 7 days**	**± 14 days**	**± 14 days**	**± 14 days**
Procedures								
Written informed consent	X							
Demographics	X							
Eligibility	X							
Hearing history	X							
Device history	X							
Medical history	X							
Unaided Audiogram – Air Conduction	X							
Unaided Audiogram – Bone Conduction	X				X			
Unaided soundfield thresholds – ear to be implanted		X						
Unaided speech perception testing in quiet – ear to be implanted – CNC words 60dBA		X						
Unaided speech perception testing in noise – ear to be implanted – BKN-SIN 65dBA		X						

Visit Type	Screening	Baseline	Surgery	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Timing of Investigation	**Day -60**	**Day -60**	**Day -0**	**Week 2**	**Week 4**	**Month 3**	**Month 6**	**Month 12**
Visit window (±) (calendar days)	NA	NA	NA	**± 7 Day**	**± 7 days**	**± 14 days**	**± 14 days**	**± 14 days**
Surgical questionnaire (including skin thickness)			X					
Aided soundfield thresholds – ear to be implanted (pre-op) OR treated ear (post-op)		X[a]			X[b]	X[b]	X[b]	
Aided speech perception testing in quiet – ear to be implanted (pre-op) OR treated ear (post-op) – CNC words 60dBA		X[a]				X[b]	X[b]	
Aided speech perception testing in noise – ear to be implanted (pre-op) OR treated ear (post-op) – BKB-SIN 65dBA		X[a]				X[b]	X[b]	
Parental questionnaire – SSQ Parent		X				X	X	
Device exposure			X	X*	X	X*	X*	X
Device programming – as needed		X			X	X	X	
Device Use Questionnaire (including hours of use)						X	X	
Concomitant medications		X	X	X	X	X	X	X
Adverse Events			X	X	X	X	X	X

[a] Baseline aided testing performed with Baha 5 Power device on a softband.
[b] Postoperative aided testing performed using the Osia 2 Sound Processor.
* Device exposure form only completed at this visit if needed.

Visit Type	Screening	Baseline	Surgery	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Timing of Investigation	**Day -60**	**Day -60**	**Day -0**	**Week 2**	**Week 4**	**Month 3**	**Month 6**	**Month 12**
Visit window (±) (calendar days)	NA	NA	NA	**± 7 Day**	**± 7 days**	**± 14 days**	**± 14 days**	**± 14 days**
Device Deficiencies				X	X	X	X	X

3 BACKGROUND INFORMATION AND RATIONALE

3.1 Introduction

The Cochlear™ Osia®2 System was cleared by the Food and Drug Administration November 15, 2019 (K191921) for individuals aged 12 years and older who present with conductive or mixed hearing loss (up to 55 dB HL) or single-sided-deafness (SSD). Published and unpublished data suggest significant pre to postoperative benefit and minimal risk in both children and adults who have received the Osia system. Due to the success of the Osia 2 system in the United States within the currently indicated patient population, clinical providers have since requested the ability to use the Osia 2 system in children aged 11 years and younger who meet the audiometric requirements. As the Osia 2 system is based on existing bone conduction and cochlear implant technologies which each possess a younger age of implantation requirement (5 years for bone conduction and 9 months for cochlear implantation), the current proposal is to align the age at implantation requirement with existing surgical bone conduction technology such as the Baha Connect and Baha Attract Systems to 5 years of age. Therefore, the objective of this study is to examine the safety and effectiveness of the Cochlear Osia 2 system in a group of pediatric subjects aged 5 to 11 years who suffer from conductive or mixed hearing loss (up to 55 dB HL), or single-sided-deafness (SSD) with the intent of expanding the indications for use.

3.2 Findings of Previous Nonclinical and Clinical Studies

3.2.1 Nonclinical Data

A summary of non-clinical data is available for reference in the Osia FDA clearance K190589.

3.2.2 Clinical Data

3.2.2.1 Data from Published Studies

Mylanus et. al. 2020 reported results from a global, multi-center, prospective, adult newly implanted clinical investigation. The study implanted 51 adult subjects across five clinical trial sites with the Osia system. The primary goals of the study were to provide evidence of both safety and effectiveness of a new bone conduction system that deploys direct piezoelectric stimulation of the bone conduction pathway to treat conductive, mixed conductive and single-sided-deafness hearing loss. Outcomes of the study at 12 months post implantation in 45 subjects demonstrated statistically significant improvements in audibility at all measured test frequencies when compared to the preoperative unaided condition. For speech recognition, study participants showed improvements in speech recognition in quiet as well as speech in noise using an adaptive speech test measure. Health utility scores as captured using the HUI-3 demonstrated statistically significant improvement when comparing the unaided to aided conditions on questions relative to hearing and speech attributes. Subjects reported significant improvements in ease of communication, reverberation and background noise on the APHAB, as well as statistically significant improvements across all domains presented in the SSQ when comparing unaided to aided outcomes. The primary safety evaluation concluded that post-operative healing was satisfactory, and few complications were reported. One implant was removed out of 51 subjects implanted due to a post-operative infection deemed not to be related to the device but to the surgical procedure.

Goycoolea et. al. 2020 reported on a cohort of 9 subjects with conductive or mixed hearing loss (8 adults and 1 child) who met the study inclusion criteria. Subjects were fit and evaluated with a Baha 5 Power sound processor on a Baha Softband compared to the aided performance using the Osia system. Post-operative evaluations were performed measuring functional gain as well as speech recognition using the Hearing in Noise Test (HINT). Patient reported outcomes were captured using the SSQ-12 and GBI questionnaires postoperatively. Surgery was deemed uneventful in all patients. Sound processor fitting was performed at 6 weeks after surgery in all patients. No skin or retention issues were observed. Overall pain scores were low indicating no or very limited pain at the initial fitting in the majority of cases with no reports of pain by 6 months post-surgery, Performance results demonstrated significant improvement in speech recognition in quiet and in noise with the Osia system as compared to the pre-operative Baha 5 Power fitting on a Baha Softband. Additionally, subjective patient reported outcomes were statistically significant pre to postoperatively.

Lau et. al. 2020 reported on the surgical and audiological outcomes using the Osia System in the first 10 United Kingdom patients. Five females and five males participated with a mean age of 52 years (range 30 – 78) who presented with either mixed (n = 5) or conductive hearing losses (n = 3) or single sided deafness (n = 2). All subjects had prior hearing aid experience and were fit with a Baha 5 Power for aided testing prior to implantation with the Osia system. Audiometrically, there was no alteration of the bone conduction thresholds post implantation. Additionally, when the subjects were segmented into the three different audiological indications, the mean gain was + 86.5 dB (range 79–94, SD = 10.6) for single-sided deafness, + 31 dB (range 12–48, SD = 17.3) for mixed and + 22 dB (range 12–31, SD = 9.5) for conductive. The mean functional gain improvement for the study population was +39.4 dB. The authors state that the enhancement in gain appeared to be one of the largest gains amongst bone conduction devices especially in the higher frequencies. Speech recognition as measured by SRT went from 38.1 dB to 22.7 dB at 4 months post-surgery. In addition to objective assessments of outcome, patient-reported outcomes measured by use of the Client Oriented Satisfaction Inventory (COSI) indicated that being able to hear well in real-life situations as well as a decrease in hearing aid disability were significant findings.

3.2.2.2 Data from Non-Published Studies

Cochlear sponsored a pediatric, newly implanted, prospective, ITA clinical trial (Cochlear CAM5706, ITA# 272423) at the Hospital for Sick Children in Toronto, Ontario, Canada. The aim of the study was to gather preliminary safety and effectiveness information on the feasibility of implanting children aged 5 years to 17 years with the Osia System. Fourteen subjects were implanted, 15 ears, aged 10 to 17 years of age with a mean age of 13.9 years who presented with either mixed or conductive hearing loss. The primary objective was to quantify the type and severity of adverse events that occurred in the study cohort. A total of 15 adverse events were recorded for the 14 subjects. All adverse events were reported as resolved by study closure. The study reported 1 serious adverse event related to a thick skin flap which prohibited the link to the external sound processor. A revision surgery to reduce the thickness of the skin flap resolved the SAE and the subject completed the study successfully. In addition to safety information, surgical questionnaires, daily use and patient reported outcomes using the SSQ-12 Parent were collected. Surgical data revealed a relatively standard procedure using a C shaped incision, general anesthesia and receipt of a 4mm BI300 implant fixture. Results of the study emphasized the importance of measuring skin flap thickness prior to implantation as well as the effectiveness of skin flap reduction in children. Daily use of the sound processor

post-operatively at six months revealed average use time of 8.4 hours daily indicating a significant use time during waking hours. Self-reported outcomes using the SSQ-12 Parent revealed a mean improvement of 2.10 for total score in the aided condition. Lastly, preliminary effectiveness data measured by both PTA 4 and speech perception in quiet using PBK monosyllabic words revealed a mean improvement in audibility of 31.7dB and a 79.1% improvement in the unaided to aided conditions respectively at 6 months postoperatively.

3.3 Study Rationale

Based on the supporting clinical evidence detailed above, the primary objective of this pivotal, multi-center, prospective, within subject, newly implanted pediatric study is to evaluate the safety and effectiveness of the Osia 2 system in children aged 5 – 11 years of age who present with conductive or mixed hearing loss (up to 55 dB HL) or single-sided-deafness (SSD). The intent of the investigation is to gather the necessary information to support a change in indications for use reducing the age at implantation to 5 years of age.

4 MEDICAL DEVICE INFORMATION

4.1 Identity and Description of the Investigational Medical Device (IMD)

The Osia 2 System is composed of the following components: the Osia Implant (OSI200); BI300 implant; and the Osia 2 Sound Processor. The Osia implant consists of a receiver/coil and an actuator/stimulator which is surgically implanted on the skull bone via a bone conduction implant surgery performed by a surgical physician trained in otolaryngology. The Osia implant connects to the BI300 implant which is secured within the skull bone. The Osia Sound Processor is an off-the-ear device, which picks up the sound from the environment, and sends the information to the implant via a transcutaneous inductive link. This link is also referred to as radiofrequency (RF) link. Each Osia System is configured to meet an individual's hearing needs, using dedicated fitting software. Because the device is commercially cleared, devices will not be labelled as investigational. The external components shall be worn full-time during waking hours. The Osia System is illustrated in Figure 1 below.

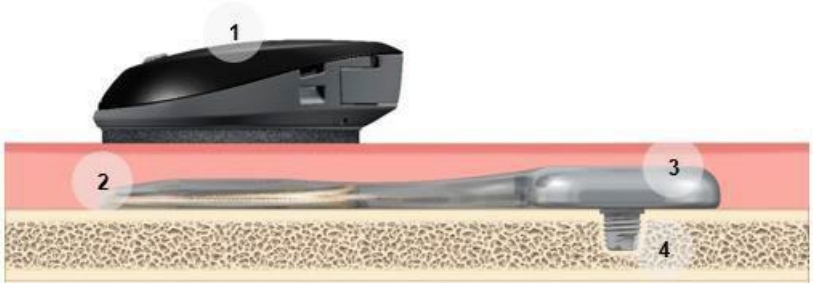

Figure 1: Overview of the Osia System, including the Osia Sound Processor

In normal operation, the Osia System functions as follows (Figure 1):

1. The external sound processor captures and digitally processes sound.
2. The sound processor transmits power and digital information to the implant coil/receiver.
3. The implant stimulator/actuator converts the digital information into an electric analogue signal that is converted to vibrations by the implant piezoelectric actuator.

4. This implant is fixed to the bone by the BI300 implant.

The actuator converts the electrical signal into an amplified mechanical stimulation, bypassing the impaired middle ear (origin of the conductive part of the hearing loss) and providing some level of mechanical amplification in order to compensate for the damaged inner ear (sensorineural part of the hearing loss, in case of mixed hearing loss).

Devices are manufactured by Cochlear Limited. For additional device information refer to the Investigator's Brochure (IB) and Instructions for Use (IFU) documents.

4.2 Identity and Description of the Comparator

Not applicable.

4.3 Accessory Device Requirements

Not applicable.

5 OBJECTIVES

5.1 Primary Objective

To demonstrate the safety of the Osia 2 System in a pediatric population aged 5 – 11 years by quantifying the type, frequency and severity of adverse events.

5.2 Secondary Objective

- To compare preoperative performance compared to postoperative performance in parental questionnaires using the Osia 2 System.
- To compare preoperative unaided bone conduction thresholds to postoperative unaided bone conduction thresholds.
- To compare unaided preoperative speech perception performance to aided speech perception performance postoperatively using the Osia 2 System.
- To compare unaided preoperative adaptive speech in noise performance to aided adaptive speech in noise performance using the Osia 2 System.

5.3 Exploratory Objective

There are no exploratory objectives.

6 DESIGN OF THE CLINICAL INVESTIGATION

6.1 General

Figure 2. Schematic for study

The clinical investigation is a pivotal, prospective, multi-center study that uses each participating subject as their own control. The study population consists of children aged 5 to 11 years of age who present with conductive or mixed hearing loss (up to 55 dB HL) or single-sided-deafness (SSD).

The intent of the study is to gather the applicable safety and effectiveness data to expand the current indications for use of the Osia 2 System to include children aged 5 years and older. The primary endpoint is to demonstrate the safety of the Osia 2 System in a pediatric population aged 5 – 11 years by quantifying the type, frequency and severity of adverse events. Secondary endpoints are to assess effectiveness of the Osia 2 System in the study population including a parental inventory, audibility, and speech perception in both quiet and noise. Data collection for endpoint assessment and all other clinical investigation measures are detailed in the Schedule of Events.

Planned study enrolment is for 50 subjects and up to 10 clinical investigation sites across the United States. Sites will be composed of both private practice and university-based hospital locations, geographically distributed across the United States who currently treat patients clinically with the Osia 2 system. Subject enrolment is anticipated to be 12 months with participation for each study subject being 14 to 18 months in duration. The Sponsor's data monitoring requirements are described in detail in a separate Monitoring Plan.

6.1.1 Design Rationale

The clinical investigation design ensures that the results obtained have clinical relevance, scientific validity and address the clinical investigation objectives. A repeated measure, within subject research design has been employed to utilize each subject as his or her own control as it accommodates the heterogeneity that characterizes hearing impaired populations. Blinding and masking are not appropriate design considerations due to the design and clinical use of the device.

Pediatric subjects seeking treatment with an Osia 2 bone conduction device may present clinically for study inclusion as being either aided or unaided due to the varying etiologies of hearing loss. Consistent with the current indications for use, subjects will be tested in both the aided and unaided listening condition to capture preoperative performance with and without a non-surgical treatment. Since the Osia 2 Sound Processor cannot be utilized in a non- surgical wearing configuration, each subject will be fit with the Baha 5 Power device on a Baha softband according to the Cochlear Baha Fitting prescription. The Baha 5 Power device is most comparable from a sound processing perspective to the Osia 2 Sound Processor. Preoperative parental inventories, tests for frequency specific audibility, as well as speech perception in quiet and noise will

be compared to performance gathered during the 3 and 6 months post-surgical evaluations to demonstrate the effectiveness of the Osia 2 system. All safety events will be gathered for Surgery plus Visits 1 – 5 and quantified by type, frequency and severity to demonstrate the safety profile for the intended study population.

6.2 Subjects

Written, informed consent must be obtained from the subject's parent or legal guardian before any study specific procedures are initiated.

A Sponsor representative (employee of Cochlear) will confirm eligibility criteria in accordance to inclusion and exclusion criteria. The representative may be either the Clinical Project Manager, a qualified ENT surgeon, audiologist or qualified subject matter expert. Following consent of a subject, the site must provide a de-identified audiogram to be reviewed by the representative.

Prior to implantation of a subject, the representative must have confirmed eligibility, and all screening and baseline assessments must be completed and entered into the EDC in accordance with the Schedule of Events.

Throughout the duration of the clinical investigation, source document records must be maintained to validate subject data.

6.2.1 Inclusion Criteria

Subjects must meet all of the inclusion criteria described below to be eligible for this clinical investigation.

1. Subjects aged 5 to 11 years of age with the following audiometric criterion:

   A conductive or mixed hearing loss and still can benefit from sound amplification. The pure tone average (PTA) bone conduction (BC) threshold (measured at 0.5, 1, 2, and 3 kHz) should be better than or equal to 55 dB HL.

   OR

   A profound sensorineural hearing loss in one ear and normal hearing in the opposite ear (i.e., single-sided deafness or "SSD"). The pure tone average air conduction (AC) hearing thresholds of the hearing ear should be better than or equal to 20 dB HL (measured at 0.5, 1, 2, and 3 kHz).

2. Prior experience with amplified sound through properly fitted amplification device such as a hearing aid, a CROS device, or a bone conduction device on a softband or sound arc.

3. Parent or legal guardian who is willing and able to provide written informed consent for the study participant.

Note: Subjects may include individuals seeking new implantation unilaterally (in one ear) or individuals already implanted with a bone-anchored device seeking a second-side implant (sequential bilateral).

6.2.2 Exclusion Criteria

Subjects who meet any of the exclusion criteria described below will not be eligible for this clinical investigation.

1. Insufficient bone quality or quantity to support implantation of both the BI300 Implant and the OSI200 Implant.
2. Chronic or non-revisable vestibular or balance disorders that could prevent benefit from the device, as determined by the investigator.
3. Abnormally progressive hearing loss.
4. Evidence that hearing loss is bilateral retro cochlear or bilateral central origin.
5. Evidence of conditions that would prevent speech recognition improvement as determined by the investigator.
6. Skin or scalp conditions that may preclude attachment of the Sound Processor or that may interfere with the use of the Sound Processor.
7. Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator.
8. Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.
9. Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of this investigation.
10. Currently participating, or participated within the last 30 days, in another clinical investigation involving an investigational drug or device that could impact the safety or effectiveness of the Osia 2 system as determined by the investigator.
11. Individuals undergoing simultaneous single-stage aural atresia or microtia repair due to the increased risk of skin complications associated with ear reconstruction.

6.2.3 Number of Subjects Required

Sample size for the study is not driven by power requirements for a formal statistical hypothesis test. The planned sample size of 50 subjects will provide data to characterize safety and effectiveness with a reasonable degree of statistical precision. Additionally, the planned sample size will allow for a high probability of observing events of interest. For example, with 50 subjects, the half-width of a two-sided 95% confidence interval for a continuous endpoint based on a t-distribution would be 0.284 units on the effect size scale. Similarly, with 50 subjects, there is a greater than 95% probability of observing one or more events that occur at a population rate of 5.9%.

Stratification of the 50 subjects will include a minimum of 10 subjects with single-sided-deafness. In addition, at least one-third (15) of the subjects represented at the youngest ages (5-6 years) will be implanted with the remaining 35 subjects represented by the other age groups as evenly as possible.

6.2.4 Vulnerable Populations

Children aged 5 to 11 years of age who present with conductive or mixed hearing loss (up to 55 dB HL) or single-sided-deafness (SSD) will be recruited for participation in this investigation. Subjects will be recruited from both private practice and university-based hospital locations, geographically distributed across the United States who currently treat patients clinically with the Osia 2 system. The clinical investigation sites will

initiate treatment as part of the study and continue care following study completion as part of standard medical and/or clinical care. Information pertaining to the study objective, visit schedule, and associated procedures will be reviewed in an age appropriate manner with both the potential subject and their parent or legal guardianprior to study participation. Verbal assent will be required for subjects aged 7 – 11 years of age and is documented according to each Institutional Review Board (IRB) requirements. Recruitment must include processes to ensure the investigator discusses the informed consent with all subjects, parent(s)or legal guardian(s) as well as addresses all questions to the individual's satisfaction. Additional measures taken to review the study with potential subjects must be documented in the informed consent process. The IRBs may have additional requirements which must be followed.

The subject's parent or legal guardian will be compensated on behalf of the subject for their time participating in the clinical investigation in alignment with fair market value, and the payment rate and process is detailed within the informed consent.

6.2.5 Recruitment and Study Duration

The following subject status definitions apply:

- Enrolled: A subject who has a signed Informed Consent form for the study.
- Screened: A subject who has a signed Informed Consent form and has met the eligibility criteria.
- Screen Fail: An enrolled subject who has been determined to not meet one or more eligibility criteria.
- Participated: An enrolled subject who has met eligibility criteria and has been treated with the Osia 2 System.
- Discontinued: An Enrolled subject who withdrew consent, was discontinued by the Investigator or Sponsor before the expected End of Study visit or was lost to follow-up. Discontinued subjects may still have safety follow-up data collection until their scheduled End of Study visit, for reasons described in section 6.2.6.
- Completed: Enrolled subjects who complete the required treatment and visit schedule.

The recruitment period for the clinical investigation is estimated to be 12 months from the time of first subject consent to recruitment of the last subject.

The expected duration of each subject's participation in the clinical investigation, is anticipated to be 14 to 18 months from the time of informed consent to End of Study Visit 5.

Clinical Investigation completion is last subject last visit. AE recording will continue for each subject until completion of their End of Study visit. Ongoing SAEs and SADEs will be followed for an additional 30 days, or until resolution or stabilization within the 30-day period following End of Study. Management of the SAE/SADE beyond clinical investigation completion will be absorbed into standard clinical and medical care by the participating clinical investigational site.

6.2.6 Criteria and Procedures for Subject Withdrawal

Subjects can decide to withdraw from the investigation at any time. The Investigator shall ask the reason(s); however, subjects have the right to withhold their reason if preferred. The reason for withdrawal should be documented in the subject's source files and the case report form (CRF), if provided.

The Investigator or Sponsor may also decide to withdraw a subject from the clinical investigation or stop the use of the investigational device if it is considered to be in the subject's best interests.

Subject withdrawal may be for any of the following reasons:

- Adverse Event (AE)
- Device Deficiency (DD)
- CIP or GCP deviation
- Subject withdrew consent
- Subject lost to follow-up
- Subject death
- Sponsor decision
- Investigator decision
- Other (specify)

If subject withdrawal is due to problems related to the safety or performance of the Osia 2 system, the Investigator may ask for the subject's permission to continue in safety follow up (for example, adverse events and device deficiencies) until their scheduled End-of-Study visit at Visit 5.

If a subject is lost to follow-up, every possible effort must be made by the study site personnel to contact the subject and determine the reason for discontinuation. At least 3 separate attempts taken to contact the subject must be documented.

Participating subjects who are withdrawn/discontinued will not be replaced.

6.2.7 Randomisation Procedures

Not applicable.

6.2.7.1 Blinding Procedures

Blinding is not an appropriate study design consideration based on the design and use of the Osia 2 System.

6.2.8 Post-investigation Medical Care

Following the investigation, subjects will continue with standard of care treatment.

6.3 Evaluations and Procedures

For each enrolled subject, the clinical investigation will include Screening and preoperative Baseline procedures, Surgery to implant the Osia 2 device, and 5 post-surgery visits.

6.3.1 Screening/eligibility

6.3.1.1 Informed Consent

Informed consent and assent, as applicable, will be obtained as outlined in section 9 of this CIP prior to any study procedures taking place.

6.3.1.2 Unaided Audiometric Testing

Unaided audiometric thresholds will be obtained for each ear independently, using the standard audiometric technique for pure-tone air and bone conduction testing preoperatively to establish candidacy for participation in the clinical investigation.

- Air Conduction: 500, 1000, 2000, 3000 & 4000Hz

Hearing thresholds that exceed the air conduction limits of the audiometer, where the participant reports feeling the acoustic stimuli, shall be recorded as vibrotactile (VT). Appropriate masking will be employed where required.

- Bone conduction: 500, 1000, 2000, 3000 & 4000Hz

Where the participant reports feeling rather than hearing the acoustic stimuli, the response shall be recorded as vibrotactile (VT). Appropriate masking will be employed where required.

For participants with conductive or mixed hearing loss, the bone conduction PTA will be captured and rounded to the nearest whole number to document audiometric eligibility. For participants with single-sided deafness (SSD), the air conduction PTA will be captured and rounded to the nearest whole number to document audiometric eligibility.

6.3.1.3 Medical, Hearing & Device History

- Hearing History will document the subject's history of hearing loss (may be subject reported) and hearing loss etiology.
- Device history will document the subject's history with hearing aids and/or surgical or non-surgical bone conduction technology (may be subject reported).
- Medical History will document the subject's medical history relevant to the conduct of the study.

6.3.2 Performance/Effectiveness

6.3.2.1 Description of Audiometric Testing

Preoperatively, unaided audiometric thresholds will also be obtained in sound field using narrowband noise. Postoperatively at Device Fitting Visit 2, unaided bone conduction thresholds will be obtained as described in section 6.3.1.2 in the implanted ear to assess the impact of implantation and aid in the fitting of the sound processor. The contralateral ear will be masked accordingly.

- Unaided Sound Field Thresholds: 500, 1000, 2000 & 4000Hz

Aided audiometric thresholds will be obtained preoperatively and in the postoperative aided condition using narrowband noise in sound field. The contralateral ear will be plugged for all tests.

- Aided Sound Field Thresholds: 500, 1000, 2000 & 4000Hz

6.3.2.2 Description of Speech Perception Testing

6.3.2.2.1 Consonant Nucleus Consonant (CNC) Monosyllabic Words

The CNC Word Test (Peterson & Lehiste, 1962) consists of 10 recorded lists of 50 monosyllabic words. For this study, one list will be administered per test condition at 60 dBA at 0º azimuth (S0) in sound field and scored as the number of phonemes and words correct, which will be expressed as a percentage correct when analyzed. Preoperatively, CNC Words will be assessed in the unaided condition as well as the aided condition using the Baha 5 Power on a softband. Postoperatively, CNC Words will be assessed only in the aided condition using the Osia 2 sound processor. Pre and postoperative testing will be completed with the contralateral ear plugged or muffed in an effort to isolate the treated ear.

6.3.2.2.2 Bramford-Kowal-Bench Speech-In-Noise (BKB-SIN)

BKB-SIN (Etymotic Research, 2005) is composed of 36 lists of BKB sentences (Bench, Kowal, & Bamford, 1979), spoken by a male target talker amidst four-talker babble. The 36 lists are divided into 18 equally difficult pairs of sentence lists. The list-pairs are composed of 16 to 20 sentences that each have 3 or 4 key words. Target speech is presented at 65 dBA and the level of the noise is varied in 3 dB steps at fixed SNRs, beginning at +21 dB SNR (very easy), and descending to 0 or –6 dB SNR (very difficult), depending on the list. Speech reception threshold (SRT) is calculated in dB, which is referred to as the SNR-50, is defined as the signal-to-noise ratio (SNR) required for the subject to repeat 50% of the key words correctly. One list pair of sentences will be presented at 0° azimuth in the sound field, with babble presented at 0º azimuth (S0N0). Preoperatively, BKB-SIN will be assessed in the unaided condition as well as the aided condition using the Baha 5 Power on a softband. Postoperatively, BKB-SIN will be assessed only in the aided condition using the Osia 2 sound processor. Pre and postoperative testing will be completed with the contralateral ear plugged or muffed in an effort to isolate the treated ear.

6.3.2.3 Description of Questionnaires

6.3.2.3.1 Speech, Spatial, and Qualities of Hearing Questionnaire (SSQ) for Parents

The Speech, Spatial, and Qualities of Hearing questionnaire (SSQ) from MRC Institute of Hearing Research, UK modified for parental response will be used as a subject self-assessment in three categories:

1. Speech hearing rating scale
2. Spatial rating scale
3. Sound qualities rating scale

6.3.2.3.2 Device Use Questionnaire (DUQ)

A Sponsor-designed Device Use Questionnaire or DUQ will be administered to the subject's parent or legal guardian to determine subjective preferences with regards to device use and satisfaction in a variety of listening environments.

6.3.3 Safety Evaluations and Procedures

Safety data will be reviewed in accordance with the Sponsor's standard operating procedures regarding safety events. The risks and anticipated ADEs for the Osia 2 system, as identified in Sections 7.2 and 7.3 below, will be assessed in the clinical investigation via reporting of all AEs/ADEs from the time of subject implantation until subject last visit. Ongoing SAEs and SADEs will be followed for an additional 30 days, or until resolution or stabilization within the 30-day period following End of Study. Management of the SAE/SADE beyond clinical investigation completion will be absorbed into standard clinical and medical care by the participating clinical investigational site.

6.3.3.1 Concomitant Medication and Therapies

Concomitant Medications recorded in the CRF includes all prescription medications, routine over-the counter medications, and any use of steroids. Medications used during surgery, vitamins, herbal and natural remedies are not included. There are no further prohibited medications under this clinical investigation. Medications taken for anesthesia purposes during surgery will not be recorded unless their use deviates from normal clinical practice.

6.3.4 Detailed Visit Schedule

6.3.4.1 Screening

- Written informed consent
- Demographics: Document date of birth and sex
- Eligibility: Confirm subject meets all inclusion criteria and no exclusion criteria. Source documentation must be available before confirming eligibility
- Hearing History: Document history of hearing loss (may be subject reported)
- Device history: Document history with hearing aids and/or surgical or non-surgical bone conduction technology (may be subject reported)
- Medical History: Document medical history
- Audiometric testing: Includes unaided air and bone conduction testing. Must be completed less than 60 days prior to implantation and document single sided deafness or mixed or conductive hearing losses.

6.3.4.2 Baseline

- Audiometric testing: Includes both unaided and aided threshold testing. Must be completed less than 60 days prior to implantation in the aided and unaided condition. The aided condition includes testing with the Baha 5 Power on a softband.
- Speech Perception testing: Includes both unaided and aided testing using CNC words and BKB-SIN sentences. Must be completed less than 60 days prior to implantation in the aided and unaided condition. The aided condition includes testing with the Baha 5 Power on a softband.

- SSQ Parent: Completed interview-style based on everyday listening condition - not aided condition with Baha 5 Power on the day of testing. Must be completed within 60 days prior to implantation.

6.3.4.3 Surgery (day 0)

- Surgical Questionnaire: documentation of surgical procedure completed day of surgery.

6.3.4.4 Visit 1: 2 Week Follow Up

- Surgical follow up: wound and incision check

6.3.4.5 Visit 2: 4 Week Device Fitting

- Bone Conduction testing: Includes unaided bone conduction threshold testing.
- Device programming: Fitting and programming of the Osia 2 sound processor.
- Sound field thresholds: Includes aided thresholds using the Osia 2 sound processor.

6.3.4.6 Visit 3: 3 Months Postoperative

- Device programming: Optional and only as needed.
- Device Use Questionnaire: Completed interview-style
- Sound field thresholds: Includes aided thresholds using the Osia 2 sound processor.
- Speech Perception testing: Includes aided testing using CNC words and BKB-SIN sentences and the Osia 2 sound processor.
- SSQ Parent: Completed interview-style based on everyday listening using the Osia 2 sound processor.

6.3.4.7 Visit 4: 6 Months Postoperative

- Device programming: Optional and only as needed.
- Device Use Questionnaire: Completed interview-style
- Sound field thresholds: Includes aided thresholds using the Osia 2 sound processor.
- Speech Perception testing: Includes aided testing using CNC words and BKB-SIN sentences using the Osia 2 sound processor.
- SSQ Parent: Completed interview-style based on everyday listening using the Osia 2 sound processor.

6.3.4.8 Visit 5: 12 Months Postoperative - End of Study

- Document Subject's study completion.
- Ensure device deficiencies, device exposure, adverse events, concomitant medications, and deviations are reviewed, and end dates recorded where appropriate.

6.3.4.9 Collected from Baseline

- Concomitant Medication: Includes all prescription medications, routine over-the counter medications, and any use of steroids. Medications used during surgery, vitamins and herbal or natural remedies are not included. Concomitant medications should be reviewed at each visit.
- Protocol Deviations: Includes approved and unapproved deviations.

6.3.4.10 Collected from Surgery

- Adverse Events: Includes initial report and review of ongoing adverse events. Adverse events should be reviewed at each visit.
- Device Exposure
- Device Deficiencies

6.4 Equipment Used for Evaluations and Procedures

The clinical investigation includes use of equipment to complete assessments. Equipment including programming software and sound equipment (e.g. speakers) are used to assess speech perception performance. Programming software should be kept current at the direction of the Sponsor. For equipment used in this clinical investigation, records of equipment calibration requirements and the calibration records for equipment used to assess Secondary Endpoint testing must be maintained in site files and copies provided to the Sponsor. As part of the Site Initiation Visit, requirements and records should be provided to the Sponsor and records confirmed to be up to date. Records will be monitored at interim monitoring visits, in accordance with the Sponsor's Monitoring Plan.

Osia Fitting Software (OFS) will be used to fit and program the Osia 2 sound processor according to patient preference. All OFS data will be provided to Sponsor for analysis, which may be done automatically or through manual file sharing.

Speech perception testing using CNC words and BKB-SIN sentences will be assessed using a loudspeaker configuration with the signal from the front, zero Azimuth (S0) at head height and 1-meter distance from the subject. The Sponsor may provide equipment (such as test materials, laptop, software, microphone and speaker) if the clinical site does not possess the necessary tools to facilitate testing.

The use of equipment will be logged and reviewed as per the Sponsor's Monitoring Plan.

6.5 Sponsor Role in Conduct of the Clinical Investigation

The Sponsor may support certain activities at the clinical investigation site. Sponsor representatives may be present in the operating room with the surgical team and subject. The representative will not provide medical assistance and will not discuss the trial with the subject.

The Sponsor may pay for third party clinical trial support ("coordinator") at clinical investigation sites should there be resource constraints, which may support subject recruitment, data entry and reporting under the authority of the Principal Investigator. The coordinator will be required to comply with hospital policy and will be trained on the CIP and GCP. The coordinator will not complete any activities on behalf of the Sponsor.

A Sponsor representative will review evidence of subject eligibility before the subject is accepted for implantation.

7 BENEFITS AND RISKS OF THE INVESTIGATIONAL MEDICAL DEVICE AND CLINICAL INVESTIGATION

7.1 Anticipated Clinical Benefits

Most recipients of a bone conduction hearing solution will experience an improved hearing performance and quality of life compared to unaided listening.

Potential benefits associated with participation in this clinical investigation include:

- Helping to find better treatments, therapies and/or diagnostic tests in the area of hearing loss or other associated conditions.
- The opportunity to be given a new intervention that may be better for their condition or that has fewer side effects or limitations than they are currently receiving.
- The opportunity to access the newest innovations in the treatment of their hearing loss type.
- Advice, care, and support from trained clinical staff who understand hearing loss and any associated conditions.
- Closer monitoring of their hearing loss.

7.2 Anticipated Adverse Device Effects

Based on the available safety reference information and literature, the potential clinical risks have been documented below.

7.2.1 Risks Associated with the Surgery

- General risks associated with surgery including pain, scarring, bleeding and infection.
- General risks associated with anesthesia during the surgery (e.g., risks for the heart, lungs, kidneys, liver, and brain) which, in rare cases, can result in death.

7.2.2 Risks Associated with Implantation of the Study Device

- Pain or discomfort
- Skin irritation near the implant, swelling or redness near the magnet site, skin breakdown
- Sense of numbness or stiffness in the area of the surgery
- Failure of the implant to properly anchor to the skull-bone due to a lack of adequate bone quantity/quality, trauma, infection, generalized diseases and surgical complications
- Other medical complications that may require additional medical treatment, such as:
  - Concurrent CSF leakage: a leak of CSF (cerebrospinal fluid) through the hole in the skull

- Subdural injury: blood vessels near the brain may burst
- Subcutaneous hematoma: bruises and contusions on the skin
- Skin-flap infection, irritation or inflammation
- Extrusion of the device caused by a foreign body under the skin
- Revision surgery to remove the study implant in the event of device failure
- Failure of the implant or sound processor could result in the perception of an uncomfortably loud sound sensation, intermittent sound, or no sound.

- The implanted magnet may affect MRI (Magnetic Resonance Imaging) procedures. The magnet may influence the MRI scanner or the ability of the scanner to detect certain changes. Under certain circumstances removal of the magnet may be necessary prior to MRI scanning.

7.2.3 Risks Associated with Use of the Study Device

- Impact or injury to the head in the area of the Osia implant could damage the implant and result in its failure. Impact to external components (e.g. sound processor) while being worn could result in damage to the device or injury. Young children who are developing motor skills are at greater risk of receiving an impact to the head from a hard object, e.g. table or chair.
- Small parts and accessories could be hazardous if swallowed and could cause choking if ingested or inhaled
- Parents and caregivers should be advised that unsupervised use of long cables (such as the safety line) may present a risk of strangulation.
- Parents and caregivers should routinely check the device for signs of overheating and for signs of discomfort or skin irritation at the implant site. Subjects should remove the processor immediately if there is any discomfort or pain (i.e., if device becomes hot or sound is uncomfortably loud) and inform their hearing care professional.

7.2.4 Risks Associated with Simultaneous Aural Atresia and Microtia Repair

When deemed appropriate by the implanting physician, a second-stage microtia/atresia reconstruction may be performed under protocol. Patients undergoing first- stage ear reconstructions in combination with Osia implantation are excluded from study participation due to the additional dissection and trauma to the area of implantation resulting in increased risk of associated skin complications. Five study subjects have undergone simultaneous aural atresia and microtia repair (3 first-stage and 2 second-stage). Two of three children who underwent first-stage ear reconstruction have required additional skin grafting on the auricle of the Medpor. The third subject experienced contact dermatitis associated with the ointment prescribed postoperatively. There have been no adverse events reported on the 2 children who underwent second-stage reconstructions.

There may also be side effects that are not known at this time.

7.3 Risks Associated with Participation in the Clinical Investigation

In addition to the anticipated surgical and adverse device effects of the Osia 2 System, the following risks may also present when participating in the clinical investigation:

- Exposure to sounds produced in the test battery that could be perceived as too loud
- Testing procedures that may produce anxiety or fatigue
- Discomfort and potential abrasion to the ear canal due to placement of insert earphones
- Discomfort associated with the fitting of the Baha 5 Power on the softband
- Possible interactions with concomitant medications and residual risks for the device are not anticipated in this clinical investigation.

7.4 Risk Mitigation

The following will be performed during the clinical investigation to mitigate the risks identified above:

- All clinical investigation sites selected have pediatric surgical bone conduction and Osia 2 system experience. The Osia 2 system being implanted is the same as the commercially cleared device currently indicated for children aged 12 years and older.
- The current surgical guidelines associated with the Osia 2 system will be reviewed during Site Initiation, specifically topics surrounding skin flap thickness and bone integrity.
- In addition, the Sponsor's surgical support may be present during surgeries performed by the investigational site(s) either in person or virtually.
- All reported AEs, ADEs and DDs will be regularly reviewed by the Sponsor's Clinical Review Board for the duration of the study to facilitate early detection and appropriate intervention if events are unanticipated with respect to incidence, severity, or outcome.
- All subject's and their parent or legal guardian will be provided with the Osia System Important Information Booklet which contains important safety warnings and cautions related to the device and its use.

7.5 Benefit-to Risk Rationale

The clinical safety (risks) and benefit relevant to the anticipated performance of the Osia 2 system were evaluated in the Osia Clinical Evaluation Report (CER) (D1179760) and it was concluded that the data reviewed provided clinical evidence for the safe and effective use of the OSI200 Implant within the Osia 2 System. Significant improvements in both objective and subjective hearing performance were observed with the device as compared to the unaided condition and resulted in an improved quality of life. The Osia 2 system has been cleared in the United States since November of 2019 for children aged 12 years and older. Cochlear-sponsored clinical investigations and a systematic literature review, coupled with the design verification/validation and post-market surveillance data, established that the benefits of the Osia 2 system outweigh the risks.

8 STATISTICAL CONSIDERATIONS

8.1 General Considerations

There is one primary endpoint and four secondary endpoints. Formal statistical hypothesis tests are planned for the secondary endpoints.

The overall type I error rate will be maintained via a gatekeeping approach whereby statistical tests will proceed in order until a non-significant test is obtained, at which point, formal testing for the purposes of labelling claims will cease. A detailed summary of statistical analysis is documented in the Statistical Analysis Plan (SAP).

8.2 Endpoints

8.2.1 Primary Endpoint

The primary endpoint is adverse events and serious adverse events Surgery through Visit 4 (6 Months). Events will be summarized by type, frequency, and severity.

8.2.2 Secondary Endpoints

8.2.2.1 Secondary endpoint 1 – SSQ Parent

Secondary endpoint 1 – SSQ Parent is defined as the mean difference between preoperative and postoperative performance on the Speech Spatial & Qualities of Hearing Questionnaire (SSQ) – Parent version at 6 months post-surgery.

8.2.2.2 Secondary endpoint 2 – PTA 4

Secondary endpoint 2 is defined as the mean difference in individual subject PTA 500, 1, 2, and 4kHz Baseline to 4 weeks post-surgery.

8.2.2.3 Secondary endpoint 3 – CNC Words

Secondary endpoint 3 is defined as the mean difference between baseline unaided speech perception in quiet and the aided condition using the Osia 2 system at 6 months post-surgery on open-set monosyllabic word recognition (CNC Words) in quiet.

8.2.2.4 Secondary endpoint 4 – BKB-SIN

Secondary endpoint 4 is defined as the mean difference between baseline unaided speech perception in noise and the aided condition using the Osia 2 system at 6 months post-surgery on an adaptive speech in noise test BKB SIN.

8.2.3 Exploratory Endpoints

There are no exploratory endpoints.

8.3 Hypotheses

8.3.1 Primary Hypothesis

There is no formal hypothesis test for the primary endpoint.

8.3.2 Secondary Hypotheses

8.3.2.1 Secondary Endpoint 1 – SSQ Parent

Secondary endpoint 1 will be assessed with the following hypothesis:

H_0: $\Delta \leq 0$

H_a: $\Delta > 0$

where Δ represents the difference between preoperative and postoperative performance on the Speech Spatial & Qualities of Hearing Questionnaire (SSQ) – Parent version at 6 months post-surgery, specifically $\Delta = SSQ_{6\ Months} - SSQ_{preop}$. This difference is parameterized so that a positive value is indicative of a clinical improvement in the questionnaire.

The hypothesis will be evaluated using a one-sample, one-sided 0.025 alpha level t-test for a mean against the null of zero. The objective will be met if the null hypothesis is successfully rejected.

The endpoint will be presented with descriptive statistics and the corresponding two-sided 95% confidence interval based on the t-distribution.

8.3.2.2 Secondary Endpoint 2 – PTA4

The secondary endpoint 2 will be assessed with the following hypothesis:

H_0: $\Delta \leq 0$

H_a: $\Delta > 0$

where Δ represents the difference between baseline PTA and 4 weeks-post surgery PTA, specifically $\Delta = PTA4_{weeks} - PTA_{preop}$. This difference is parameterized so that a positive value is indicative of a clinical improvement.

The hypothesis will be evaluated using a one-sample, one-sided 0.025 alpha level t-test for a mean against the null of zero. The objective will be met if the null hypothesis is successfully rejected.

The endpoint will be presented with descriptive statistics and the corresponding two-sided 95% confidence interval based on the t-distribution.

8.3.2.3 Secondary Endpoint 3 – CNC Words

The secondary endpoint 3 will be assessed with the following hypothesis:

H_0: $\Delta \leq 0$

H_a: $\Delta > 0$

where Δ represents the difference between baseline unaided speech perception CNC and 6 months-post surgery CNC, specifically $\Delta = CNC_{6\ Months} - CNC_{preop}$. This difference is parameterized so that a positive value is indicative of a clinical improvement.

The hypothesis will be evaluated using a one-sample, one-sided 0.025 alpha level t-test for a mean against the null of zero. The objective will be met if the null hypothesis is successfully rejected.

The endpoint will be presented with descriptive statistics and the corresponding two-sided 95% confidence interval based on the t-distribution.

8.3.2.4 Secondary Endpoint 4 – BKB-SIN

The secondary endpoint 4 will be assessed with the following hypothesis:

H_0: $\Delta \leq 0$

H_a: $\Delta > 0$

where Δ represents the difference between baseline unaided speech perception BKB SIN test and 6 months-post surgery BKB SIN test, specifically $\Delta = BKB_{6\ Months} - BKB_{preop}$. This difference is parameterized so that a positive value is indicative of a clinical improvement.

The hypothesis will be evaluated using a one-sample, one-sided 0.025 alpha level t-test for a mean against the null of zero. The objective will be met if the null hypothesis is successfully rejected.

The endpoint will be presented with descriptive statistics and the corresponding two-sided 95% confidence interval based on the t-distribution.

8.3.3 Exploratory Hypothesis

There are no exploratory hypotheses.

8.4 Sample Size Determination

Sample size for the study is not driven by power requirements for a formal statistical hypothesis test. The planned sample size of 50 subjects will provide data to characterize safety and effectiveness with a reasonable degree of statistical precision. Additionally, the planned sample size will allow for a high probability of observing events of interest. For example, with 50 subjects, the half-width of a two-sided 95% confidence interval for a continuous endpoint based on a t-distribution would be 0.284 units on the effect size scale. Similarly, with 50 subjects, there is a greater than 95% probability of observing one or more events that occur at a population rate of 5.9%.

Stratification of the 50 subjects will include a minimum of 10 subjects with single-sided-deafness. In addition, at least one-third (15) of the subjects represented at the youngest ages (5-6 years) will be implanted with the remaining 35 subjects represented by the other age groups as evenly as possible.

8.5 Analysis Populations

Analysis will be based on subjects who are successfully implanted with the device.

8.6 Endpoint Analyses

8.6.1 Primary Endpoint Analyses

There is no formal hypothesis test for the primary endpoint.

The endpoint will be presented in tabular format, displaying the number and percentage of subjects with adverse events. Events will also be summarized by type and severity. Results will be based on observed events without imputation.

8.6.2 Secondary Endpoint Analyses

The secondary endpoint (1 – 4) analyses will be presented with descriptive statistics and the corresponding two-sided 95% confidence interval based on the t-distribution.

8.6.3 Exploratory Endpoint Analyses

There are no exploratory endpoints.

8.7 Safety Analyses

Adverse events (AEs) will be tabulated with the number of events and subjects with event for each event type and overall. Rates will be reported as the number of subjects who experience at least one event during the analysis interval out of the total number of subjects with follow-up to the beginning of the analysis interval. Serious adverse events (SAEs) will also be tabulated.

All AEs and SAEs will also be summarized by relatedness as described above. Adverse events leading to death or study discontinuation will be provided in listing format.

8.8 Interim Analyses

No formal interim analyses for the purposes of early stopping for effectiveness or for adaptive sample size re-estimation are planned. Periodic reports on study progress may be reported to regulatory agencies. Regulatory submission is planned following the collection of the 6-month study data. Data through 12 months will be considered supplemental.

9 INFORMED CONSENT PROCESS

The Investigator shall obtain written informed consent from the subject's parent or legal guardian using an approved ICF prior to any clinical investigation-related examination or activity. The rationale of the clinical investigation, as well as the benefits and risks, what participation will involve, and established alternatives to participation will be explained to the subject and their parent or legal guardian in native non-technical language, understandable to the subject. Ample time will be provided for the subject and parent or legal guardian to enquire about details of the clinical investigation and to decide whether to participate.

All questions about the clinical investigation shall be answered to the satisfaction of the subject or the subject's parent or legal guardian. Subjects shall not be coerced or unduly influenced to participate or to continue to participate in a clinical investigation. They shall not waive or appear to waive their legal rights.

Each subject's parent or legal guardian, and the person who conducted the informed consent discussion, shall sign and personally date the Informed Consent Form (ICF). Where required, an independent and impartial witness shall sign and personally date the ICF. A copy of the signed ICF shall be given to the subject. The original signed ICF shall be archived in the Investigator's Site File or subject file at the investigational site.

This process shall be documented in the subject's source documents.

The subject and the subject's parent or legal guardian, shall be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the clinical investigation. The communication of this information must be documented as an update to the ICF and re-consent of the subject.

10 ADVERSE EVENTS AND DEVICE DEFICIENCIES

10.1 Definitions

10.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons whether or not related to the medical device or the procedures required for implant or use, and whether anticipated or unanticipated.

NOTE 1: This definition includes events related to the medical device or the comparator device.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users and other persons, this definition is restricted to events related to the use of medical devices.

10.1.2 Adverse Device Effect

An adverse device effect (ADE) is an AE related to the use of a medical device.

NOTE 1: This includes any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the medical device.

NOTE 3: This includes 'comparator' if the comparator is a medical device.

10.1.3 Serious Adverse Event

A serious adverse event (SAE) is any AE that led to any of the following:

1) death,
2) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:

- a life-threatening illness or injury, or

- a permanent impairment of, or damage to, a body structure or a body function including chronic diseases, or
- in-patient hospitalisation or prolonged hospitalisation, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment or damage to a body structure or a body function,

3) foetal distress, foetal death or a congenital physical or mental abnormality, or birth defect including physical or mental impairment.

NOTE: Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a SAE.

10.1.4 Serious Adverse Device Effect

A serious adverse device effect (SADE) is an ADE that has resulted in any of the consequences characteristic of a SAE.

10.1.5 Unanticipated Serious Adverse Device Effect

An unanticipated serious adverse device effect (USADE) is a SADE, which by its nature, incidence, severity, or outcome has not been identified in the current version of the IB and IFU.

A USADE is also known as a UADE (Unanticipated Adverse Device Effect) for the purposes of US FDA reporting.

NOTE: An anticipated serious adverse device effect is an effect, which by its nature, incidence, severity, or outcome has been identified in the IB and IFU.

10.1.6 Adverse Events of Special Interest

There are no adverse events of special interest for this clinical investigation.

10.1.7 Device Deficiency

A Device Deficiency (DD) is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

NOTE 1: Device Deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling.

NOTE 2: This definition includes device deficiencies related to the IMD or the comparator.

10.1.8 Serious Health Threat

A signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons.

NOTE: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

10.2 Recording and Handling of Adverse Events

Subjects shall be carefully monitored during the clinical investigation and the investigator should enquire about AEs at investigation visits.

All AEs will be recorded from the time of implantation. AE recording will continue for each subject until completion of their End of Study visit. Ongoing SAEs and SADEs will be followed for an additional 30 days, or until resolution or stabilization of the event, whichever comes first. Management of the SAE/SADE beyond clinical investigation completion will be absorbed into standard clinical and medical care by the participating clinical investigational site.

Source notes should indicate the evaluation for AEs, even if there was none to report. All required AEs will be reported if observed, even if anticipated and/or acknowledged as a risk factor in the consent.

All AEs will have the following information documented: start and stop dates, action taken, outcome, severity and investigators opinion on the potential relationship to the Osia 2 system and study procedures. If an AE changes in severity, the most severe (highest) grade will be captured for that event on the Adverse Events CRF.

10.2.1 Assessment of Severity

The Principal Investigator (or qualified delegate) will make an assessment of severity for each event based on clinical judgement. The intensity of each event recorded in the CRF should be assigned to one of the following categories:

Mild	An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
Moderate	An event that is sufficiently discomforting to interfere with normal activities
Severe	An event which is incapacitating and prevents normal everyday activities

10.2.2 Assessment of Causality

The Investigator will assess the potential causal relationship of each event, using clinical judgement. Alternative causes, such as natural history of underlying diseases, other risk factors and the temporal relationship of the event to the Osia 2 system will be considered and investigated. The causal relationship to the Osia 2 system is to be assessed by the Investigator (or medically qualified delegate) and should be assessed using the following classifications:

Not related	Relationship to the medical device or procedures can be excluded when: • the event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has no temporal relationship with the use of the device or the procedures; • the event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;

	• the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event; • the event involves a body-site or an organ not expected to be affected by the device or procedure; • the event can be attributed to another cause (for example, an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); • the event does not depend on a false result given by the investigational medical device used for diagnosis, when applicable; • harms to the subject are not clearly due to use error; In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.
Unlikely related	The relationship with the use of the medical device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possibly related	The relationship with the use of the medical device is weak but cannot be ruled out completely. Alternative causes are also possible (for example, an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possibly related.
Probably related	The relationship with the use of the medical device seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.
Definitely related	The event is associated with the medical device or with procedures beyond reasonable doubt when: • the event is a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has a temporal relationship with the medical device use/application or procedures; • the event involves a body-site or organ that – the medical device or procedures are applied to – the medical device or procedures have an effect on; • the event follows a known response pattern to the medical device (if the response pattern is previously known); • the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible); • other possible causes (for example, an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out; • harm to the subject is due to error in use; • the event depends on a false result given by the medical device used for diagnosis, when applicable; In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.

10.2.3 Assessment of Seriousness

The Investigator will assess the seriousness of each event according to clinical judgement and the definition provided in section 10.1.3.

10.2.4 Assessment of Expectedness

An event should be considered unanticipated if the nature, severity, or frequency of that event is not consistent with the applicable safety reference information, such as the hazards analysis, IB, or Product Information/IFU if the product is approved for marketing.

For this clinical investigation the listed items in Section 7.2 and 7.3 of this CIP and/or the instructions for use (IFU) cleared for the Osia 2 system are anticipated ADEs.

Anticipated	An adverse device effect (ADE) which by its nature, incidence, severity, or outcome is consistent with the applicable safety reference information (for example, IB, IFU).
Unanticipated	An adverse device effect (ADE) which by its nature, incidence, severity, or outcome is not consistent with, or has not been identified in the applicable safety reference information (for example, IB, IFU).

10.2.5 Non-reportable Adverse Events

Any adverse events (AEs) that are experienced by study subjects prior to implantation will not be recorded or reported.

10.3 Recording and Handling of Device Deficiencies

Subjects shall be carefully monitored during the clinical investigation and routinely questioned about DDs at investigation visits. Source notes should indicate the evaluation for DDs, even if there are none to report.

The Investigator shall assess if the DD led to an AE or could have led to a serious medical occurrence (serious adverse device effect) if;

1) suitable action had not been taken,
2) intervention had not been made, or,
3) circumstances had been less fortunate

All DDs will be documented in the source notes and the DD page of the CRF. As the study device is a commercially cleared product, the standard commercial returns process applies.

10.4 Reporting Responsibilities

The Investigator is responsible for reporting all AEs and DDs in the CRF.

10.4.1 Investigator Reporting of Serious Adverse Events

All AEs meeting the criteria for an SAE, or DD that could have led to an SADE must be reported to the Sponsor in a timely manner. Reporting is achieved through completion of the events details in the Adverse Event page of the eCRF.

The Investigator shall always provide an assessment of causality at the time of the initial report, as described in section 10.2.2 'Assessment of Causality'. If data obtained after reporting indicates that the assessment of causality is incorrect, then the SAE form may be appropriately amended, signed, dated, and resubmitted to the Sponsor.

If the Investigator does not have all other information regarding an SAE, he/she will not wait to receive additional information before reporting the event. The reporting forms shall be updated when additional information is received.

The Investigator is responsible for reporting of safety events to their local EC using the applicable report form, in accordance with local regulations.

10.4.2 Sponsor Notification of Events

The Sponsor is responsible for reviewing all safety data to evaluate potential causality and anticipation of all ADEs, and shall conduct an expedited assessment of all SAEs, unanticipated ADEs, DDs that could have led to a SADE, including serious health threat.

The Sponsor is also responsible for reporting all reportable events according to the requirements and timelines of the regulatory authorities relevant to this clinical investigation. Country specific sponsor reporting responsibilities are outlined in the Sponsor's Safety Data Handling Plan.

The Safety Monitor for AE/DD assessment and any AE/DD related queries is:

Name Sponsor Safety Monitor:	[redacted]
Country:	
Phone number:	
E-mail:	

10.5 Independent Data Monitoring Committee

An Independent Data Monitoring Committee (IDMC) will be established to provide an independent review of safety and compliance outcomes for this clinical investigation. The IDMC will review trial data and provide recommendations to the Sponsor regarding the course of the clinical investigation. The scope of the IDMC and its associated procedures will be outlined in the IDMC Charter.

11 Device Accountability

Subject level device supply will be tracked using the Individual Subject Device Accountability Log Form (1295295).

As the device under investigation is cleared within current indications, device traceability from Sponsor to Site will be tracked through the commercial distribution process and the Sponsors local work instruction. Packing lists will be stored in the site files for reference.

Additionally, the Osia 2 system should be registered by the investigational site with the Sponsor according to the commercial registration practices as the devices remain with the subjects following the conclusion of the clinical investigation. If during the course of the trial, a repair or return is required, the investigational site and Sponsor will adhere to the commercial Return Material Authorization (RMA) process. Similarly, in the event a device requires explantation, the investigational site and the Sponsor will adhere to the commercial process in place for the return of explanted devices.

At the end of the clinical investigation, if the investigational site is in possession of any unused devices, all product should be returned to the Sponsor according to the commercial RMA process.

Further detail regarding device accountability tracking and storage will be detailed in the Monitoring Plan.

Contact information regarding the Osia 2 system is provided below.

Name of contact person of the Sponsor:	[redacted]
Country and time zone:	
Phone number:	
Email:	

12 DEVIATIONS FROM THE CLINICAL INVESTIGATION PLAN

The Investigator(s) must not deviate from the CIP, except in case of an emergency to protect the safety and well-being of the subject(s). Such deviations will be documented by the site personnel in the source documentation for the subject and reported to the relevant EC as per institutional requirements and to the Sponsor as soon as possible, but not later than 5 working days from the date of the emergency. Per 21 CFR 812.25(b) Sponsor is required to report emergency deviations to the FDA within 5 working days of notification of the event.

If there is a deviation from CIP-defined assessments or parts thereof are omitted or completed incorrectly, the deviation will also be documented by the site personnel in the source documentation for the subject. Depending on the type or severity of the deviation the Investigator may be required to notify the EC, particularly if the deviation potentially impacts subject safety, performance of [IMD][and/or comparator], or data integrity.

All CIP deviations will be documented in the eCRF to enable analysis and reporting by the Sponsor in the Clinical Investigation Report (CIR), or to the relevant regulatory authority(s), if applicable.

Gross misconduct on behalf of an Investigator, such as intentional non-compliance with CIP or GCP requirements or fraud, will result in disqualification of the Principal Investigator and/or Investigational Site from participation in the investigation. Data provided by the Principal Investigator or Investigational Site will be excluded from the per-protocol analysis group.

13 DATA MANAGEMENT

The CRF will capture the datapoints necessary to determine the subject status according to the criteria described in section 6.3.

13.1 Source Data

An Origin of Source Data Form will be used to capture the location of source data kept at each site, outlining the individual site's process for certification.

Source data will be captured in clinic notes, paper-based source data worksheets, or printed directly from testing software. As indicated on the Origin of Source form, data collected may be entered directly into the eCRF which shall be considered source data for these items. If electronic medical records do not permit read only access for monitoring purposes, a certified printout must be provided, indicated by a dated signature by a member of the site team or generated through a validated process.

13.2 Methods for Data Entry and Collection

Data collection will be performed using [redacted] for electronic data capture (EDC) on electronic Case Report Forms (eCRFs). Site staff will be trained on the completion of the eCRFs prior to obtaining access to the system and will have their own Login/Password. Access to clinical study information will be based on an individual's role and responsibilities.

[redacted] uses role-based user permissions for data entry, viewing, and reporting options. All communications between users and the EDC server are encrypted. Web servers are protected by a managed firewall. This application is designed to be in compliance with applicable regulations including 21 CFR Part 11.

The application will include programmed data consistency checks and supports manual generation of data clarifications/queries, including documentation of site responses. This application maintains a comprehensive audit trail for all data entered, including updates and queries, and documents the time that each entry occurred and who made the entry.

Principal Investigators will affirm that the data for each subject at their site is accurate and complete by way of an electronic signature.

In addition, de-identified electronically generated data will be collected from the Osia Fitting Software. The unamended data file shall be regarded as the source.

13.3 Database Lock

The database will be locked upon the completion of collection of data from Visit 4 6-months and again at the completion of the study.

The process for database lock is described in the Data Management Plan.

14 CONFIDENTIALITY

The investigator and site staff will collect and process personal data of the subjects in accordance with governing data privacy regulations, including Good Clinical Practices (GCPs) and with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Data will be reported to the Sponsor on CRFs or related documents (for example, questionnaires). Subjects will be identified on CRFs and other related documents only by a unique subject identification code and shall not include the subject's name or other personal identifiable information. Completed CRFs or related documents are confidential and will only be available to the Investigator and site staff, the Sponsor and their representatives, and if requested to the Ethics Committee and national regulatory authorities. Publications or submission to a regulatory authority shall not disclose the identity of any subject.

15 ETHICS COMMITTEE AND REGULATORY AUTHORITY APPROVAL

The clinical investigation will not commence prior to the written favourable opinion or approval from the EC and regulatory authority is obtained.

The final Sponsor-approved version of the CIP, Informed Consent Form, and other necessary documents shall be submitted to the EC. A copy of the EC opinion/approval shall be provided to the Sponsor.

The Investigator shall forward to the Sponsor, for review and approval, any amendment made to the approved ICF and any other written information to be provided to the subject prior to submission to the EC.

The Sponsor and Principal Investigator will continue communications with the EC, as required by national regulations, the clinical investigational plan, or the responsible regulatory authority.

Any additional requirements imposed by the EC or regulatory authority will be implemented by the Sponsor.

The Investigator shall submit the appropriate documentation if any extension or renewal of the EC approval is required. In particular, substantial amendments to the CIP, the ICF, or other written information provided to subjects will be approved in writing by the EC.

The Investigator shall report to the EC any new information that may affect the safety of the subjects or the conduct of the clinical investigation. The Investigator will send written status summaries of the investigation to the EC regularly, as per local EC requirements.

Upon completion of the clinical investigation, the Investigator shall provide the EC with a brief report of the outcome of the clinical investigation, as per local EC requirements.

The clinical investigation is covered by clinical trial insurance, meeting the requirements of the participating countries.

16 SUSPENSION OR PREMATURE TERMINATION

The Sponsor will discontinue the clinical investigation site if:

1) major non-adherence to the CIP or GCP principles is occurring
2) it is anticipated that the subject recruitment will not be adequate to meet the objectives of the clinical investigation

An ongoing clinical investigation may be discontinued in case of:

1) device failure
2) serious or intolerable ADE, leading to the explant or discontinued use of the device
3) subject's death

In the event of premature study termination, the subjects will continue to be managed clinically by their medical provider.

17 AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

Sponsor will notify all site Principal Investigators of changes to the CIP. No changes in the CIP or investigation procedures shall be made without mutual agreement of the Principal Investigator and the Sponsor. This agreement will be documented as a CIP amendment. Amendments will require notification to the Ethics Committees (ECs) by the Principal Investigators and to the relevant regulatory authority(s) by the Sponsor.

18 RECORD KEEPING AND RETENTION

Data generated from the clinical investigation will be stored in a limited-access file area and be accessible only to representatives of the study site, the Sponsor and its representatives, and relevant health authorities/regulatory agencies. All reports and communications relating to study subjects will identify subjects only by subject unique identification code. Complete subject identification will be maintained by the Investigator. This information will be treated with strict adherence to professional standards of confidentiality.

Per 21 CFR 812.140 (d), an investigator or sponsor shall maintain the records required by this subpart during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, OR the date that the records are no longer required for purposes of supporting a premarket approval application, a notice of completion of a product development protocol, a humanitarian device exemption application, a premarket notification submission, or a request for De Novo classification.

The Sponsor will notify the Principal Investigator when records are no longer needed. The Investigator will not discard any records without notifying the Sponsor. If the Principal Investigator moves from the current investigational site, the Sponsor should be notified of the name of the person who will assume responsibility for maintenance of the records at the investigational site or the new address at which the records will be stored. The Investigator will notify the Sponsor as soon as possible in the event of accidental loss or destruction of any study documentation.

19 PUBLICATION POLICY

This clinical investigation will be prospectively registered at a public clinical trial registry, ClinicalTrials.gov.

A joint peer-reviewed publication authored by the clinical investigator(s) and Sponsor will be prepared. In addition, the results of the clinical investigation may also be disseminated as conference presentations (for example, abstract and poster session). Manuscript authorship and responsibilities will be discussed and agreed upon prior to investigation start and in accordance with guidelines and recommendations provided by

the International Committee of Medical Journal Editors (ICMJE) to enable communication within 12 months of the Clinical Investigation Report (CIR) approval. All contributors who do not meet the criteria for authorship will be listed in an acknowledgments section of the publication.

20 STATEMENTS OF COMPLIANCE

This clinical investigation shall be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, International Standard ISO 14155:2020 Clinical investigation of medical devices for human subjects - Good Clinical Practice, 21 CFR Parts 812, 50, 54, 56 & 11, and any other regional or national regulations, as applicable.

21 QUALITY CONTROL AND ASSURANCE

In accordance with Cochlear's Quality Management System, all clinical investigations shall be conducted according to internationally recognised ethical principles for the purposes of obtaining clinical safety and performance data about medical devices.

The Sponsor employees (or designee) shall use standard operating procedures (SOPs) to ensure that clinical study procedures and documentation are consistently conducted and compliant with the ISO 14155 Standard, Good Clinical Practice (GCP), and applicable local regulations as noted in section 20 above.

21.1 Monitoring

The Sponsor will perform on-site and remote monitoring visits as frequently as necessary to oversee conduct, data collection and record keeping by sites. The clinical investigation monitoring plan is a separate document for the sponsor to follow, describing all the activities performed during site qualification, initiation, monitoring, and close out.

In accordance with applicable regulations, GCP, and sponsor's/CRO's procedures, monitors will contact the site prior to the start of the study to review with the site staff the CIP, study requirements, and their responsibilities to satisfy regulatory, ethical, and sponsor's requirements. When reviewing data collection procedures, the discussion will also include identification and documentation of source data items.

The sponsor/designee will monitor the site activity to verify that the:

- Data are authentic, accurate and complete
- Safety and rights of subjects are being protected
- Study is conducted in accordance with the currently approved CIP
- Any other study agreements, GCP, and all applicable regulatory requirements are met.

The investigator and the head of the medical institution (where applicable) agrees to allow the monitor direct access to all relevant documents.

21.2 Audits

To ensure compliance with GCP, the CIP, study procedures and applicable regulatory and EC requirements, an independent audit of the study may be conducted. The investigator/institution will be informed of the outcome for audits involving their site.

In addition, inspections by regulatory health authority representatives and EC(s) are possible. An Investigator must, in reasonable time, upon request from a relevant health authority or regulatory agency, permit access to requested records and reports, and copy and verify any records or reports made by the Investigator. Upon notification of a visit by a regulatory authority, the Investigator will contact the Sponsor immediately.

The Investigator will grant the Sponsor representatives the same access privileges offered to relevant health authority or regulatory agents, officers, and employees, for the purposes of a Sponsor audit of the site, or in preparation for an inspection.

Audits and inspections may occur at any time during or after completion of the study.

22 TRADEMARKS AND COPYRIGHT

23 REFERENCES

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24 CHANGE HISTORY.

Version	Change	Rationale
1	Initial Release	NA
2	Changed references of Approved Medical Device on Test (AMDT) to Investigational Medical Device (IMD)	Due to internal requirements on the classification of the devices that is being studied outside of approved indications.
3	Revised sections 9.2.2.2 and 9.3.2.2 regarding secondary endpoint PTA being collected at 4-weeks post-surgery	Error noted in the body of the document regarding the timing of this secondary endpoint; correct in the synopsis
4	Migrated to new template. Added references to relevant parts of 21 CFR for compliance. Changed Legally Authorized Representative to Legal Guardian throughout. Commercial labelling and device manufacturing information added to section 5.1. Withdrawn changed to discontinued in section 7.2.5. Screening/eligibility section added to section 7.3. Greater descriptions of screening requirements included. Description of the Device Use Questionnaire included in section 7.3.2.3. Updated detailed visit descriptions to include that the questionnaires are completed interview-style. Removed visit windows section 7.4.3. Added risks to study device use in section 8.2.3. Added risk mitigation for risks to study device use in section 8.4. Updated adverse event and device deficiency definitions. Added definition of Serious Health Threat in section 11.1.8. Added section 11.2.5 Non-Reportable Adverse Events. Section 12 updated for explant return procedures. Section 12 updated to change contact person. Section 14 updated to include database lock procedures. Section 22.1 expanded with further monitoring details. Exclusion criteria added. Risks of simultaneous procedures incorporated added in section 8.2.4.	New template released to reflect changes required from the ISO 14155:2020 update. Clarified items to reflect actual practice. Update to study personnel. FDA recommendations

Version	Change	Rationale
5	Change in study safety monitor. Update to formatting for section 6 header. Updated applicable section references throughout the document.	Change in study personnel. Error in formatting in previous version. Errors found in references.

APPENDICES

APPENDIX 1: STATEMENT/DECLARATION OF DEVICE CONFORMITY