Official Title: A post-market interventional cohort study evaluating the clinical efficacy of the Osia 2 system in the US Market

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Clinical Investigation Plan

A post-market interventional cohort study evaluating the clinical efficacy of the Osia 2 system in the US Market.

Short Tile:	Osia CPT Code Study
CIP Number:	CAM5778
Version Number:	3.0
Date:	19-June-2020
Sponsor:	Cochlear Americas 10350 Park Meadows Drive Lone Tree, CO 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 Clinical investigation of medical devices for human subjects - Good Clinical Practice, and any regional or national regulations, as applicable.

Manufacturer	Cochlear Bone Anchored Solutions AB Konstruktionsvägen 14 PO Box 82 435 22 Mölnlycke Sweden Tel: 031- 792 44 74
Sponsor Organizations	Cochlear Americas 10350 Park Meadows Dr Lone Tree, CO 80124
Contract Services	[redacted]
Safety Contact	[redacted]

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.

Name	**Title**
Site Name	**Site Address**
Signature	**Date**

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1 DEFINITIONS AND ABBREVIATIONS

Term	Description
ADE	Adverse Device Effect
AE	Adverse Event
AMDT	Approved Medical Device on Test
CER	Clinical Evaluation Report
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CRF	Case Report Form
DCF	Data Clarification Form
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
EOS	End of Study
GCP	Good Clinical Practices
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
NCA	National Competent Authority
PI	Principal Investigator
PIL	Principal Investigator List
PMS	Post-Market Surveillance
SADE	Serious Adverse Device Effect

Term	Description
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A post-market interventional, cohort study evaluating the clinical efficacy of the Osia 2 system in the US Market.
Short title	Osia 2 CPT Code Study.
Investigation number	CAM 5778
Name of investigational medical device(s)	Osia 2 Active Osseointegrated Implant System for Bone Conduction.
Intended use of investigational medical device(s)	Treatment of conductive and mixed conductive hearing loss in adults aged 18 years and older with bone conduction PTA4 (.5, 1, 2, and 3kHz) better than or equal to 55 dBHL in the treated ear.
Name and description of comparator device/product(s)	Reference device: Baha 5 Power sound processor on the Baha Sound Arc.
Expected start date (first subject consented)	July 2020
Expected enrolment period	6 – 8 months.
Expected duration per subject	7 – 8 months.
Expected total duration of the clinical investigation	12-18 months.
Number of subjects planned	Up to 20 Newly Implanted Osia 2 subjects.
Number of investigational sites planned	Up to 6 US sites.
Inclusion criteria	• Willing and able to provide written informed consent. • Proficient in English. • Hearing loss etiology of Conductive or Mixed Conductive loss. • Bone conduction PTA (.5, 1, 2, and 3kHz) better than or equal to 55dB HL in the treatment ear. • Aged 18 years and older.

Exclusion criteria	• Unwilling to wear the treatment device or comply with the surgical and rehabilitation requirements of the study. • Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator. • Medical, audiological or psychological conditions, as judged by the investigator that might contraindicate participation in the clinical investigation. • 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 contractors engaged by Cochlear for the purposes of this investigation. • Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device. • Prior experience with a surgical bone conduction treatment option. • Insufficient bone quality to support the BI300 implant as determined by the surgeon.
Primary objective(s)	To evaluate the performance of the Osia 2 system on an adaptive speech in noise test.
Secondary objective(s)	To evaluate the safety of the Osia 2 system in a group of adult newly implanted recipients.
Exploratory objective(s)	Not applicable.
Primary endpoint(s)	To demonstrate significant difference between the aided and unaided conditions at 3 months using an adaptive speech in noise test when compared to the preoperative (Visit 1) unaided condition.
Secondary endpoint(s)	To evaluate the safety of the Osia 2 system in a group of adult newly implanted recipients by estimating the incidence of device or procedure related adverse events.
Exploratory endpoint(s)	Not applicable.

3 SCHEDULE OF EVENTS

	Screening	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6 EOS
Timing of Investigation	**Day -1**	**Day -1**	**Day 0**	**Week 2**	**Week 4**	**Month 3**	**Month 6**
Visit window (±)	**NA**	**± 0 days**	**± 0 days**	**± 5 days**	**± 7 days**	**± 7 days**	**± 7 days**
Time Estimation	**2 hrs. 15 mins.**	**3 hrs. 15 mins**	**1 hr.**	**1 hr.**	**3 hrs.**	**4 hrs.**	**3 hrs.**
Written informed consent	X						
Demographics	X						
Inclusion/Exclusion	X						
Hearing history	X						
Medical history	X						
Audiogram	X						
Concomitant Medications[1]		X	X	X	X	X	X
Sound field thresholds		X[2]			X[3]	X[4]	X
Speech perception testing in quiet		X[5]			X[6]	X[7]	X

[1] Collected post-Visit 1 only if changes to prescription concomitant medications associated with device or procedure-related adverse event.
[2] Includes sound field thresholds, unaided and aided, with Baha 5 Power on Sound Arc.
[3] Visits 4 & 6 include sound field thresholds, aided, with Osia Sound Processor.
[4] Visit 5 includes sound field thresholds, unaided and aided, with Osia Sound Processor.
[5] Includes speech in quiet testing, unaided and aided, with Baha 5 Power on Sound Arc.
[6] Visits 4 & 6 include speech perception in quiet, aided, with Osia Sound Processor.
[7] Visit 5 includes speech perception in quiet, unaided and aided, with Osia Sound Processor.

	Screening	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6 EOS
Timing of Investigation	**Day -1**	**Day -1**	**Day 0**	**Week 2**	**Week 4**	**Month 3**	**Month 6**
Visit window (±)	**NA**	**± 0 days**	**± 0 days**	**± 5 days**	**± 7 days**	**± 7 days**	**± 7 days**
Time Estimation	**2 hrs. 15 mins.**	**3 hrs. 15 mins**	**1 hr.**	**1 hr.**	**3 hrs.**	**4 hrs.**	**3 hrs.**
Speech perception testing in noise +5 dB SNR		X[8]				X[9]	
Adaptive speech in noise testing		X[10]			X[11]	X[12]	X
SSQ 12		X				X	
Patient Reported Questionnaire		X				X	
Device Counseling		X			X		
Surgical Follow up				X			
Fitting and Optimization of Sound Processor		X[13]			X[14]	X	X
Device Deficiencies			X	X	X	X	X
Adverse Events			X	X	X	X	X
Data Entry	X	X	X	X	X	X	X

[8] Includes speech perception in noise, unaided and aided, with Baha 5 Power on Sound Arc.
[9] Visit 5 includes speech perception in noise, unaided and aided, with Osia Sound Processor.
[10] Includes adaptive speech in noise testing, unaided and aided, with Baha 5 Power on Sound Arc.
[11] Visit 4 & 6 include adaptive speech in noise testing, aided, with Osia Sound Processor.
[12] Visit 5 includes adaptive speech in noise testing, unaided and aided, with Osia Sound Processor.
[13] Fitting with Baha 5 Power on Sound Arc.
[14] Fitting with Osia Sound Processor.

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

Bone conduction implant systems are designed to provide aural rehabilitation for individuals with moderate to severe conductive (CHL) or mixed (MHL) hearing losses or single-sided sensorineural deafness (SSD). The initial bone conduction system relied on percutaneous transmission of sound vibrations from an electromagnetic transducer connected to a skin-penetrating abutment attached to an osseointegrated screw-shaped fixture. Due to the efficient transmission pathway and availability of a range of powerful sound processors, percutaneous implants continue to offer the broadest audiological fitting range and remain the most commonly used bone conduction implant type. In recent years, there has been rapid development of new implantable transcutaneous options for patients in need of a bone conduction hearing solution that maintain efficient transmission but also reduce complication rates due to the percutaneous abutment.

The Osia System is a new active transcutaneous implant system that uses piezoelectric instead of electromagnetic stimulation and is built on the experience gained from both transcutaneous and percutaneous bone conduction systems. The implanted piezoelectric element fixes to bone via an osseointegrated implant similar to current percutaneous devices. The digital sound signal is transferred from the sound processor to the implant through a digital radio frequency (RF) link. Due to this design, the Osia system is able to provide a more efficient transmission of sound, especially in the high frequency range, as the implantable transducer eliminates the attenuation of sound vibrations through soft tissue that is inherent to passive bone conduction systems. The additional high frequency output aids consonant recognition and word discrimination ultimately improving auditory comprehension, especially in noisy environments.

Clearance for the Osia 2 system was supported by a global clinical trial evaluating safety and efficacy in a mixed, mixed conductive and single-sided deaf adult population. Fifty-one (51) adult subjects were included in the investigation and a total of 53 devices were implanted across five investigational sites. The overall study duration per subject was 12 months post implantation with the primary efficacy time point at 3 months post implantation and primary safety at 6 months post implantation. The results are detailed in the Clinical Investigation Report for study CBAS5539 Clinical performance of a new implant system for bone conduction hearing Document No: D1478473.

Upon clearance of the Osia 2 system in the United States, it was determined that the clinical evidence intended to support the reimbursement coverage of the Osia 2 system was inadequate. To further support the reimbursement efforts associated with the Osia 2 system, clinical evidence gathered in the United States will be collected.

4.1.1 Nonclinical Data

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

4.1.2 Clinical Data

The outcomes from CBAS5539 Clinical performance of a new implant system for bone conduction hearing are available in Document No: D1478473.

4.2 Study Rationale

As it was determined that the clinical evidence intended to support the reimbursement coverage of the Osia 2 system was inadequate, clinical evidence gathered in the United States will be collected to further support the reimbursement efforts associated with the Osia 2 system.

5 MEDICAL DEVICE INFORMATION

5.1 Identity and Description of the Approved Medical Device on Test (AMDT)

The Osia System is made up of several components. The Osia Implant (OSI200) consists of a receiver/stimulator and an actuator (vibrator) which is surgically implanted on the skull bone. The external component of the Osia System is a sound processor, worn off-the-ear, which picks up the sound from the environment, and sends, after processing, 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. The Osia System is illustrated in Figure 1 below.

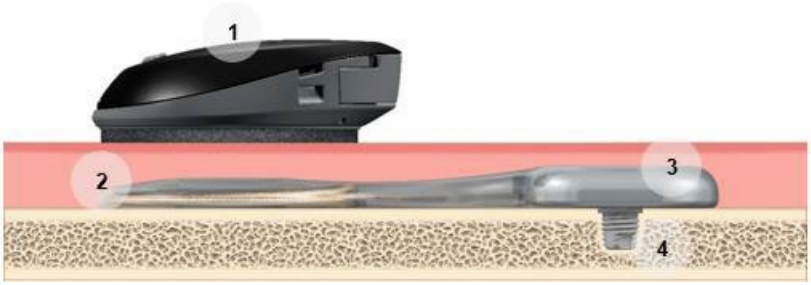

Figure 1: Overview of the Osia System, including the Osia Sound Processor

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).

5.2 Identity and Description of the Comparator

The Baha 5 Power will be utilized on a Sound Arc as the pre-surgical reference for the aided test condition. Each subject will be assessed in both the aided and unaided condition pre-operatively and then compared to their performance aided and unaided at the 3 months post- surgical test visit using the AMDT, the Osia 2 system. The signal processing of the Baha 5 Power is most comparable to the Osia Sound Processor and therefore has been chosen as the comparator.

5.3 Accessory Device Requirements

Not applicable.

6 OBJECTIVES

6.1 Primary Objective

To evaluate the performance of the Osia 2 system on an adaptive speech in noise test.

6.2 Secondary Objective

To evaluate the safety of the Osia 2 system in a group of adult newly implanted recipients.

6.3 Exploratory Objective

Not Applicable.

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

A post-market interventional cohort study evaluating the clinical efficacy of the Osia 2 system in the US Market.

The subjects include adults aged 18 years and older who meet the pre-specified study inclusion and exclusion criteria. Up to 20 eligible subjects will be enrolled.

Study subjects will be implanted with the Osia 2 system according to the commercially approved Physicians Guide. Subjects will attend scheduled study visits as described in the CIP Schedule of Events (Section 3). At study visits, subjects will undergo hearing and safety assessments. The primary endpoint is to evaluate the performance of the Osia 2 system on an adaptive speech in noise test. Safety associated with implantation of the Osia 2 system will be assessed by recording and summarizing device or procedure related AEs and DDs. No data monitoring committee will be used for this clinical investigation. An analysis will be conducted once all subjects complete Visit 5. All subjects will attend an End-of-Study visit at the time they complete the study.

7.1.1 Design Rationale

This clinical investigation design ensures that the results obtained have clinical relevance, scientific validity and address the clinical investigation objectives. A 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.

Subjects seeking treatment with an Osia 2 bone conductive device may present clinically as being aided or unaided, therefore it is important to capture both listening conditions to ensure a representative sample. 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 Sound Arc 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.

A test order randomization paradigm has been employed to minimize test order effects and demonstrate the unaided to aided benefits of bone conduction technology. Due to the physiology of a conductive or mixed conductive hearing loss, there are no carry-over effects associated with the use of an osseointegrated bone conduction intervention and therefore comparisons can be made.

7.2 Subjects

7.2.1 Inclusion Criteria

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

investigation.

- Willing and able to provide written informed consent.
- Proficient in English.
- Hearing loss etiology of Conductive or Mixed Conductive loss.
- Bone conduction PTA (.5, 1, 2, and 3 kHz) better than or equal to 55 dB HL in the treatment ear.
- Aged 18 years and older.

7.2.2 Exclusion Criteria

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

- Unwilling to wear the treatment device or comply with the surgical and rehabilitation requirements of the study.
- Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator.
- Medical, audiological or psychological conditions, as judged by the investigator that might contraindicate participation in the clinical investigation.
- 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 contractors engaged by Cochlear for the purposes of this investigation.
- Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device.
- Prior experience with a surgical bone conduction treatment option

Insufficient bone quality to support the BI300 implant as determined by the surgeon

Written, informed consent must be obtained from the subject before any study procedures are initiated.

7.2.3 Number of Subjects Required

A total of up to 20 newly implanted subjects is planned. This sample size should provide adequate power for statistical tests of the primary endpoint under conservative assumptions.

7.2.4 Vulnerable Populations

Not applicable.

7.2.5 Enrollment & Study Duration

The following subject status definitions apply:

Consented: A subject who has provided informed consent and is being assessed for eligibility according to the Screening requirements.

Screen Fail: A consented subject that has been determined to not meet all eligibility criteria for enrolment.

Enrolled/Treated: Subjects who have met all eligibility criteria, have qualified for surgery and have received the Osia 2 implant.

Withdrawn: Enrolled subjects who withdraw or are withdrawn by the Investigator or Sponsor before their expected end of study visits. Withdrawn subjects may still continue in safety follow-up until their scheduled end of study visit for reasons described in section 7.2.6.

The enrollment period for the clinical investigation is anticipated to be 6 - 8 months from the time of first subject consent to enrollment of the last subject.

The expected duration of each subject's participation is 7-8 months.

During this time there will be required research related visits.

- Screening
- Visit 1
- Visit 2: Surgery - Treatment
- Visit 3: 2-week check post-surgery
- Visit 4: 4-week post-surgery fitting
- Visit 5: 3 Months post-surgery
- Visit 6: 6 Months post-surgery (End of Study)

The anticipated total duration of the clinical investigation is therefore 12 - 18 months including set up, execution and closure. The execution phase of the Clinical Investigation is considered complete after the last subject, last visit. IRBs should remain open through closeout monitoring activities, until Sponsor notifies site of database lock.

7.2.6 Criteria for Subject Withdrawal

Subjects can decide to withdraw from the investigation at any time. The Investigator shall ask the reason(s). The reason for withdrawal should to be documented in the subject's source files and the case report form (CRF).

The Investigator or Sponsor may also decide to withdraw a subject from the clinical investigation if it is considered to be in their best interests.

Subject withdrawal may be for any of the following reasons:

- Adverse Event (AE)

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

If subject withdrawal is due to problems related to the AMDT or comparator safety or performance, the Investigator shall ask for the subject's permission to continue in safety follow up (i.e., adverse events) until their scheduled End-of-Study visit.

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 may be documented in the medical chart.

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

7.2.7 Randomization Procedures

Subjects who meet eligibility criteria for enrolment will be randomized to a test order for the 3-month interval prepared by the Sponsor. Subjects will be randomly assigned to one of two test order configurations using a ratio of 1:1.

7.2.8 Blinding Procedures

Not applicable for the current clinical investigation.

7.2.9 Post-investigation Medical Care

Not applicable for the current clinical investigation.

7.3 Performance Evaluations and Procedures

7.3.1 Metrics

7.3.1.1 Audiometric Thresholds

7.3.1.1.1 Unaided audiometric thresholds

Unaided audiometric thresholds will be obtained for each ear, with insert earphones or headphones, using the standard audiometric technique for pure-tone air-conduction testing. All preimplantation testing will be completed using an audiometer calibrated to American National Standards Institute (ANSI) standards with maximum output for frequencies of 0.5 to 4 kHz. Pure tone threshold exploration will be completed using the adaptive Hughson &

Westlake procedure[1].

Testing in each ear will include the following:

Air conduction thresholds: 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz with appropriate masking as required;

Bone conduction thresholds: 250, 500, 1000, 2000, 3000 & 4000 Hz with appropriate masking as required.

NOTE: An audiogram completed up to 90 days prior to Screening will be considered valid for determination of eligibility and data collection as part of Screening if all required frequencies detailed above were assessed.

7.3.1.1.2 Aided audiometric thresholds

Aided audiometric thresholds will be obtained in a calibrated sound field, using the standard audiometric technique for sound field testing. The purpose of this assessment is to establish hearing thresholds in the free-field through a speaker in the front position (0º azimuth). All testing will be completed using narrow band noise in a sound field calibrated to American National Standards Institute (ANSI) standards with maximum output for frequencies of 0.5 to 4 kHz. The test shall be performed with the non-test ear blocked. Testing will include the following:

Aided sound field thresholds: 500, 1000, 2000, 4000, 6000Hz.

7.3.1.2 Speech perception in quiet

7.3.1.2.1 CNC Monosyllabic Words

The CNC Word Test[2] is a validated test used clinically and in research to assess the performance of adults with hearing loss on open-set word recognition. The test consists of 10 recorded lists of 50 monosyllabic words in CD format. Two lists will be administered in quiet at a level equal to 60 dBA in the sound field and scored as total number of words and phonemes correct, which will be expressed as a percentage correct for this study. Subjects will be tested using a configuration of speech at 0º azimuth in quiet (S0). The test shall be performed with the non-test ear blocked. Visit 1 will be performed in the unaided and aided condition using the Baha 5 Power on a Sound Arc. Visits 4, 5, and 6 will be performed using the Osia 2 Sound Processor.

7.3.1.3 Speech perception in noise

7.3.1.3.1 AzBio Sentences in Noise

The AzBio Sentence Test[3] is a validated test used clinically and in research to assess the open- set sentence recognition in speech-weighted noise of adults with hearing loss. It consists of 15 lists of 20 sentences each. AzBio sentences are spoken by different talkers in a conversational style with limited contextual cues that the listener can use to predict or ‘fill in’ unintelligible words. The sentences will be presented at a fixed level of 65 dBA at a fixed

+5 dB signal-to-noise ratio (SNR) using the accompanying noise stimulus. Each list includes

5 sentences from 4 different male and female speakers. The average level of intelligibility of each list is 85% +/- 1%. Each word in the sentence counts towards the overall score (percent correct). Subjects will be tested using a configuration of speech and noise at 0º azimuth (S0N0). The test shall be performed with the non-test ear blocked. Visit 1 will be performed in the unaided and aided condition using the Baha 5 Power on a Sound Arc and Visit 5 will be performed using the Osia 2 Sound Processor.

7.3.1.3.2 QuickSin

The QuickSin[4] was developed to provide a quick way for clinicians to quantify a patient's ability to hear in noise, determine if extended high frequency emphasis improves or degrades understanding of speech in noise and provide a large number of equivalent test lists for use in clinical and research work. Each track consists of six sentences with five key words per sentence presented in four-talker babble noise. The sentences are presented at signal-to- noise ratios which will be decreased manually in 5-dB steps from 25 (very easy) to 0 (extremely difficult). The SNRs used are: 25, 20, 15,10, 5 and 0, encompassing normal to severely impaired performance in noise. Subjects will be tested on 4 individual tracks (24 sentences) at 65dB(A) using a configuration of speech at 0º and noise at 180º azimuth (S0N180) for each condition. The split noise tracks are numbered 24 – 35. The test shall be performed with the non-test ear blocked. Visit 1 will be performed in the unaided and aided condition using the Baha 5 Power on a Sound Arc. Visits 4, 5, 6 will be performed using the Osia 2 Sound Processor.

7.3.1.4 Speech, Spatial, and Qualities of Hearing Scale (SSQ-12)

The short form of Speech, Spatial, and Qualities of Hearing questionnaire (SSQ-12)[5] from MRC Institute of Hearing Research, UK, is a scaled-down version of the 49-item SSQ questionnaire. It is designed to compile a sub-set of items from the longer original 49-item version to represent the scale as a whole, measuring self-reported auditory disability, reflecting the reality of hearing in the everyday world.

Categories of assessment include:

- Hearing speech in a variety of competing contexts.
- The directional, distance and movement components of spatial hearing.
- Segregation of sounds and attending to simultaneous speech streams.
- Ease of listening.
- The naturalness, clarity, and identifiability of different speakers, different musical pieces and instruments, and different everyday sounds.

The SSQ-12 will be completed in the everyday listening condition at Visit 1 and Visit 5.

7.3.1.5 Patient Reported Questionnaire

The Patient Reported Questionnaire is an in-house developed questionnaire designed to collect subjective ratings on each subject's experiences with their current technology. The Patient Reported Questionnaire will be completed in the everyday listening condition at Visit

1 and Visit 5.

7.3.1.6 Medical History

Medical history CRFs will be collected at Visit 1. Information collected will include current or past medical or surgical conditions relevant to the conduct of the study.

7.3.1.7 Hearing History

Hearing history will be collected at Visit 1. Information collected will include duration, type and etiology of hearing loss in addition to any non-surgical hearing loss treatment details (e.g. hearing aid use).

7.3.2 Methods

7.3.2.1 Screening and Informed Consent

Subjects who have been deemed appropriate candidates for implantation according to standard clinical practice will be considered potential research subjects for this study. Informed consent must occur prior to study related activities with the exception of an audiogram performed within 90 days of Screening/Candidacy. Individuals will be appropriately counselled on the risks and benefits of study participation prior to participating in any study related activity. The risks of surgery shall be explained to the subjects as outlined in the Informed Consent Form. After reviewing the Informed Consent Form, the candidate will be given the opportunity to review and ask questions about the Informed Consent Form and/or the study prior to signing the Informed Consent Form. The candidates will be offered the opportunity to take the form home to discuss with family members should they choose to do so. If the participant agrees to participate, a copy of the executed informed consent will be provided to the participant. All individuals who provide informed consent will be assigned a unique identifier. A unique alphanumeric code will identify each subject throughout the course of the study.

7.3.2.2 Screening Visit

Subjects are consented into the study and the following data should be collected on all subjects who meet eligibility criteria. The only required documentation for subjects who do not meet eligibility criteria at the Screening visit is the Informed Consent Form and Eligibility electronic Case Report Form.

7.3.2.2.1 Electronic Case Report Forms

- Inclusion/Exclusion – Eligibility
- Demographics
- Hearing history
- Medical history
- Device History

7.3.2.2.2 Audiometric testing

Testing in each ear will include the following:

- Unaided air conduction thresholds: 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz with appropriate masking as required
- Unaided bone conduction thresholds: 250, 500, 1000, 2000, 3000, 4000 Hz with appropriate masking as required

7.3.2.3 Visit 1

7.3.2.3.1 Electronic Case Report Forms

- Concomitant Medications - See section 7.2.4 below for additional information.

7.3.2.3.2 Sound field hearing thresholds – 500, 1000, 2000, 4000 and 6000 Hz

- Unaided
- Aided with Baha 5 Power on a Sound Arc.

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.3.3 CNC Word Test (Speech perception testing in quiet) – 2 lists 60dB(A) in sound field - S0

- Unaided
- Aided with Baha 5 Power on a Sound Arc

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.3.4 AzBio Sentence Test in Noise – 1 list 65 dB(A) +5dB SNR in sound field – S0N0

- Unaided
- Aided with Baha 5 Power on a Sound Arc

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.3.5 QuickSin Test – 4 lists 65 dB(A) in sound field – S0N180

- Unaided
- Aided with Baha 5 Power on a Sound Arc

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.3.6 Patient Reported Outcomes

- SSQ-12
- Patient Reported Questionnaire

7.3.2.4 Visit 2: Surgery

Subjects will be implanted with a commercially cleared Osia 2 system according to the surgical technique detailed in the Physicians Guide. Surgery is considered treatment, and thus the start of adverse event reporting.

7.3.2.5 Visit 3: 2 Week Post Surgery

Subjects will be seen for a 2-week post-surgical follow up to ensure the incision and implant site are healing appropriately in preparation for fitting at 4 weeks post- surgery. If applicable, device or procedure related adverse events and device deficiencies will be collected during this visit.

7.3.2.6 Visit 4: 4 Week Post Surgery

7.3.2.6.1 Fitting

- Optimization of the Osia 2 Sound Processor and device counselling

7.3.2.6.2 Sound field hearing thresholds – 500, 1000, 2000, 4000 and 6000Hz

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.6.3 CNC Word Test (Speech perception testing in quiet) – 2 lists 60dB(A) in sound field - S0

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.6.4 QuickSin Test – 4 lists 65 dB(A) in sound field – S0N180

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.7 Visit 5: 3 Months Post Surgery

7.3.2.7.1 Sound field hearing thresholds – 500, 1000, 2000, 4000 and 6000 Hz

- Unaided
- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.7.2 CNC Word Test (Speech perception testing in quiet) – 2 lists 60dB(A) in sound field - S0

- Unaided
- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.7.3 AzBio Sentence Test in Noise – 1 list 65 dB(A) +5dB SNR in sound field – S0N0

- Unaided
- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.7.4 QuickSin Test – 4 lists 65 dB(A) in sound field – S0N180

- Unaided
- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.7.5 Patient Reported Outcomes

- SSQ-12
- Patient Reported Questionnaire

7.3.2.8 Visit 6: 6 Months Post Surgery, End of Study

7.3.2.8.1 Sound field hearing thresholds – 500, 1000, 2000, 4000 and 6000Hz

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.8.2 CNC Word Test (Speech perception testing in quiet) – 2 lists 60dB(A) in sound field - S0

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed.

7.3.2.8.3 QuickSin Test – 4 lists 65 dB(A) in sound field – S0N180

- Aided with Osia 2 Sound Processor

Note: The test shall be performed with the non-test ear plugged/muffed

7.3.3 Safety Evaluations and Procedures

The identified risks and anticipated device related adverse events detailed in Sections 8 and 11 of the CIP will be assessed in the clinical investigation via reporting of all device and procedure related AEs/ADEs. Reporting timeframe will start for each individual subject at the time of treatment and end at either subject withdraw or completion in the study.

Safety data adjudication may be conducted by the Sponsor's Medical Officer in accordance with the Sponsor's standard operating procedures.

7.3.4 Concomitant Medication and Therapies

A comprehensive list of concomitant prescription medications will be captured in subjects who meet eligibility at the screening visit. Medications available over the counter will not be collected. Changes to concomitant prescription medications associated with device or procedure related adverse events will also be captured throughout the course of the trial.

7.4 Equipment Used for Evaluation of Performance and Safety

The following equipment will be used to evaluate performance and safety:

- Audiometers: data collected on this equipment will be used for candidacy determination and screening as well as postoperative assessments.

- Sound booth: location where a subject will be assessed. The sound booth will be outfitted with two speakers.
- Calibration records should include audiometer, insert earphones and/or headphones and sound field environment.

No other equipment calibration records will be required for this clinical investigation.

7.5 Sponsor Role in Conduct of the Clinical Investigation

Sponsor representatives may be present for intraoperative surgical support and clinical support of programming visits.

Sponsor representatives will be actively engaged in monitoring and operational communications with clinical sites for appropriate oversight and to ensure compliance. Further details regarding site communications and roles/responsibilities are documented in the Safety Data Handling Plan and Communications Plan.

To mitigate any potential bias, if it is requested that the Sponsor enter data into the electronic data capture system, the assigned individuals will not be involved in analysis of data. The Clinical Project Manager as well as the Clinical Review Board will be tasked with reviewing data listings for any abnormal trends associated with protocol compliance and/or safety issues. Formal analyses will be performed according to the Statistical Analysis Plan.

8 RISKS AND BENEFITS OF THE CLINICAL INVESTIGATION AND APPROVED MEDICAL DEVICE ON TEST

8.1 Anticipated Clinical Benefits

Potential benefits associated with participation in the clinical investigation include:

- Helping to find better treatments, therapies and/or diagnostic tests in the area of hearing loss or other condition
- 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 receiving now
- The opportunity to access the newest innovations in the treatment of hearing loss
- The chance to play an active role in their own hearing health and gain a greater understanding of their condition
- Advice, care, and support from trained clinical staff who understand hearing loss or their condition
- Closer monitoring of their hearing loss or condition

8.2 Anticipated Adverse Device Effects

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

8.2.1 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

8.2.2 Additional 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 AMDT may be necessary prior to MRI scanning.
- There may be side effects that are not known at this time.

8.3 Risks Associated with Participation in the Clinical

Investigation

In addition to the anticipated surgical and adverse device effects of the AMDT, 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 Sound Arc

8.4 Risk Mitigation

The clinical investigation sites chosen for participation in the study have been previously trained as part of the Sponsors Controlled Market Release (CMR). Each have experience treating the indicated population with the AMDT.

The study design introduces minimal risk outside of the standard commercial risks associated with bone conduction technology. Additionally, all reported device or procedure related adverse events and device deficiencies captured during the course of the study will be regularly reviewed by the Sponsor's Clinical Review Board to facilitate early detection and appropriate intervention if events are unanticipated with respect to incidence, severity, or outcome. Device associated adverse events and deficiencies will also be entered into our Global Quality Complaint Management System to allow for post market trending and any applicable reporting to regulatory authorities.

8.5 Risk-to-Benefit Rationale

The subjects recruited for this study are already considering treatment with an osseointegrated bone conduction device. The risk benefit rationale is such that participation in this study will provide subjects with additional hearing health information pertaining to their outcome with the Osia 2 bone conduction system than they would receive commercially.

9 STATISTICAL CONSIDERATIONS

9.1 General Considerations

Except where otherwise specified, the following general principles apply to the planned statistical analyses. All statistical analysis will be conducted using [redacted] or other widely-accepted statistical or graphical software as required.

Continuous data will be summarized with mean, standard deviation, median, minimum,

maximum, and number of evaluable observations. Categorical variables will be summarized with frequency counts and percentages. Confidence intervals may be presented, where appropriate, using the t-distribution for continuous data and Clopper-Pearson Exact method for categorical variables.

All investigational sites will follow the requirements of a common protocol and standardized data collection procedures and forms. All efforts will be put forth to ensure near complete follow-up, with particular focus on the assessment of the primary outcome and occurrence of adverse events. Regular reminders of subject follow-up due dates will be provided to participating centers to facilitate scheduling of follow-up visits. Further details regarding statistical considerations can be found in the Statistical Analysis Plan.

9.2 Endpoints

9.2.1 Primary Endpoint

To demonstrate significant difference between the aided and unaided conditions at 3 months using an adaptive speech in noise test when compared to the preoperative (Visit 1) unaided condition.

9.2.2 Secondary Endpoint

The secondary endpoint is to evaluate the safety of the Osia 2 system in a group of adult newly implanted recipients by estimating the incidence of device or procedure related adverse events.

9.2.3 Exploratory Endpoints

There are no exploratory endpoints.

9.3 Hypotheses

Formal hypothesis tests are planned for the primary endpoint to establish superiority of the aided over unaided conditions. Statistical hypothesis tests will be based on t-tests with a one-sided 0.025 alpha level.

9.3.1 Primary Hypothesis

The primary objective is to evaluate the performance of the Osia 2 system on an adaptive speech in noise test. A t-test of superiority for the adaptive speech in noise test, comparing the aided and unaided conditions at 3-months relative to the preoperative (Visit 1) unaided condition. The mathematical statement of this hypothesis test is written as:

H0: $\Delta On \geq \Delta Off$ H1: $\Delta On < \Delta Off$

where ΔOn is the mean change in the adaptive speech in noise test between the 3-month aided (on) condition and the preoperative unaided condition, and ΔOff is the mean change in the adaptive speech in noise test between the 3-month unaided condition (off) and the

preoperative (Visit 1) unaided condition. Successful rejection of the null hypothesis indicates the aided performance of the Osia 2 system is superior to the unaided performance based on the adaptive speech in noise test.

9.3.2 Secondary Hypothesis

There is no secondary hypothesis as the intent is to capture the observed rate of incidence for device and procedure related adverse events.

9.3.3 Exploratory Hypothesis

There are no exploratory hypotheses.

9.4 Sample Size Determination

The planned sample size of 20 will provide greater than 95% power under a conservatively assumed mean of 12 and standard deviation of 15. Calculations are based on a one-sided 0.025 alpha and include allowance for attrition of up to 20%.

9.5 Analysis Populations

Analysis will be based on the intent-to-treat population. In order to obtain a complete ITT population, multiple imputation will be used for any missing outcome data.

9.6 Primary Endpoint Analyses

Analysis of the primary endpoint will be based on a paired t-test of means comparing the change from preoperative (Visit 1) between the 3-month aided and unaided conditions. This will be a superiority test based on a one-sided 0.025 alpha level. Sensitivity analyses will include testing for a period and for a crossover effect.

9.7 Secondary Endpoint Analyses

Descriptive statistics, specifically counts and percentages of device or procedure related adverse events captured through 6 months post-surgery, will be summarized.

9.8 Exploratory Endpoint Analyses

There are no exploratory hypotheses.

9.9 Safety Analyses

Descriptive statistics, specifically counts and percentages of device or procedure related AEs, will be summarized for the subject population. Any subjects who die, are treatment

failures, or discontinued an intervention due to an adverse event will be summarized separately.

9.10 Interim Analysis

Analysis will be conducted upon completion of Visit 5 (3 months post-surgery) or once the minimum sample size requirements are met for the primary endpoint.

10 INFORMED CONSENT PROCESS

The Investigator shall obtain written informed consent from the subject using an approved ICF prior to any clinical investigation-related examination or activity. The rationale of the clinical investigation, as well as the risks and benefits, what participation will involve, and alternatives to participation will be explained to the subject. Ample time will be provided for the subject 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 legally acceptable representative. Subjects shall not be coerced or unduly influenced to participate or to continue to participate in a clinical investigation.

Each subject and the person who conducted the informed consent discussion, shall sign and date the Informed Consent Form (ICF). Where required, a 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.

The subject 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.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 Definitions

11.1.1 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.

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 medical devices.

11.1.2 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.

11.1.3 Serious Adverse Event

A serious adverse event (SAE) is any AE that:

a) led to a death,

b) led to a serious deterioration in the health of the subject that either resulted in:

- a life-threatening illness or injury, or
- a permanent impairment of, or damage to, a body structure or a body function, or
- in-patient hospitalization or prolonged hospitalization, 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, or
- Chronic disease.

c) led to fetal distress, fetal death or a congenital physical or mental abnormality, or birth defect

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

11.1.4 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.

11.1.5 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 instructions for use (IFU).

USADE are 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 IFU.

11.1.6 Adverse Events of Special Interest

Adverse Events of Special Interest are not applicable for this clinical investigation.

11.1.7 Device Deficiency

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

NOTE: Device Deficiencies include malfunctions, use errors, and inadequate labelling or information supplied by the manufacturer.

11.2 Recording and Handling of Adverse Events

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

All ADEs, SAEs and UADEs associated with the AMDT will be recorded from the time of treatment with the AMDT through each individuals' last study visit. Ongoing ADEs, SADEs or UADEs at the time of study completion will be transitioned to ongoing clinical management.

It is recommended that source notes indicate the evaluation for AEs, even if none to report. All required device or procedure related AEs will be reported if observed, even if anticipated and/or acknowledged as a risk factor in the consent.

All required AEs will have the following information documented: start and stop dates, action taken, outcome, severity and investigators opinion on the potential relationship to the AMDT 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.

Events that include the typical stages of wound healing without additional medical intervention beyond the standard of care are not required to be reported for adverse device or procedure events.

11.2.1 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.

11.2.2 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 AMDT will be considered and investigated. The causal relationship to the AMDT 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 (e.g. 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 (e.g., 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 (e.g., 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.

11.2.3 Assessment of Seriousness

The Investigator will assess the seriousness of each event according to clinical judgement.

11.2.4 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 risk analysis report, hazards analysis, IB, or Product Information/IFU if the product is approved for marketing.

For this clinical investigation the listed items in Section 8 of this CIP and/or the instructions for use cleared for this AMDT are considered anticipated ADEs.

Anticipated	An adverse device effect (ADE) which by its nature, incidence, severity, or outcome is consistent with the applicable safety reference information (e.g., 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 (e.g., IB, IFU).

11.3 Recording and Handling of Device Deficiencies

Subjects shall be carefully monitored during the clinical investigation and routinely questioned about DDs at investigation visits. It is recommended that source notes indicate the evaluation for DDs, even if none to report.

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

a) suitable action had not been taken,

b) intervention had not been made, or,

c) circumstances had been less fortunate

All DDs associated with the AMDT will be documented on the DD page of the CRF.

11.4 Reporting Responsibilities

The Investigator is responsible for reporting all AEs and DDs according to the requirements of the CIP in the CRF.

11.4.1 Investigator Reporting of Serious Adverse Events

All device or procedure related AEs meeting the criteria for an SAE, or DD that could have led to a 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. If data obtained after reporting indicates that the assessment of causality is incorrect, then the AE form may be appropriately amended, signed, dated, and resubmitted to the Sponsor.

If the Investigator does not have all other information regarding an ADE, SADE or UADE, 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.

11.4.2 Sponsor Notification of Events

The Sponsor is responsible for reviewing all safety data to evaluate potential causality and anticipation of all ADEs.

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, and shall conduct an expedited assessment of all SADEs, unanticipated ADEs, and DDs.

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

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

11.5 Independent Data Monitoring Committee

An Independent Data Monitoring Committee (IDMC) will not be established for this clinical investigation as it encompasses both product and indications cleared within the current indications for use.

12 DEVICE ACCOUNTABILITY

As the device and subject population under investigation is cleared within the current indications for use (i.e., approved medical device on test (AMDT)) including any comparators, device traceability from Sponsor to Site will be tracked through the commercial distribution process. Packing lists will be stored in the site files for reference.

Additionally, AMDT's and comparators 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.

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.

Subject level device supply will be tracked using the Sponsor's Individual Subject Accountability Log Form. Further detail regarding device accountability tracking and storage will be detailed in the Monitoring Plan.

Contact information regarding the AMDT is provided below.

Name of contact of Clinical Project Manager:	[redacted]
Country and time zone:	[redacted]

Phone number:	[redacted]
Email:	[redacted]
Name and contact of Clinical Research Associate:	[redacted]
Country and time zone:	[redacted]
Phone number:	[redacted]
Email:	[redacted]
Name and contact of Clinical Research Associate:	[redacted]
Country and time zone:	[redacted]
Phone number:	[redacted]
Email:	[redacted]

13 DEVIATIONS FROM THE CLINICAL INVESTIGATION PLAN

The Investigator(s) should 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. 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 AMDT, 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.

14 DATA MANAGEMENT

The CRF will capture subject status according to the following criteria:

- Consented: Signed consent and eligibility evaluations underway

- Screen Fail: Subject determined not to be eligible to proceed for participation
- Enrolled/Treated: Subjects who are considered enrolled or treated have been successfully implanted with the AMDT. Any participant who is not successfully implanted will be considered a treatment failure and classified accordingly.
- Withdrawn: Enrolled subjects who withdraw or are withdrawn by the Investigator or Sponsor before the expected End of Study visit.
- Complete: Enrolled subjects who complete the planned follow up schedule and End of Study visit.

Source data will be captured in clinic notes, paper-based source data worksheets, or printed directly from testing software. The Origin of Source Form will be completed for each site prior to first subject consented, to support clear and concise identification of source data at each clinical site. If electronic medical records do not permit read only access for monitoring purposes, a verified printout and/or certified copy must be provided.

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. The 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 clinical fitting software. The unamended data file shall be regarded as the source.

15 CONFIDENTIALITY

The investigator and site staff will collect and process personal data of the subjects in accordance with governing data privacy regulations [such as the EU GDPR regulations].

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.

16 ETHICS COMMITTEE AND REGULATORY AUTHORITY APPROVAL

The clinical investigation will not commence prior to the written favorable opinion or approval from the EC and or regulatory authority (if appropriate) 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.

17 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.

18 AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

Sponsor will notify all site Principal Investigators of changes to the CIP. 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, if applicable).

19 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.

20 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 (e.g., 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 in a timely manner. All contributors who do not meet the criteria for authorship will be listed in an acknowledgments section of the publication.

21 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 Clinical investigation of medical devices for human subjects - Good Clinical Practice, and any regional or national regulations, as applicable.

22 QUALITY CONTROL AND ASSURANCE

In accordance with Cochlear's Quality Management System, all clinical investigations shall be conducted according to internationally recognized 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 (SOP) 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.

22.1 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 describing all the activities performed during site qualification, initiation, monitoring, and close out.

22.2 Audits

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.

23 TRADEMARKS AND COPYRIGHT

24 REFERENCES

1) Hughson W, Westlake HD. Manual for program outline for rehabilitation of aural casualties both military and civilian. Trans Am Acad Ophthal Oto-lar. 1944(Suppl.):3-15.

2) Peterson GE, Lehiste I. Revised CNC lists for auditory tests. The Journal of speech and hearing disorders. 1962;27:62-70.

3) Spahr AJ, Dorman MF, Litvak LM, Van Wie S, Gifford RH, Loizou PC, et al. Development and validation of the AzBio sentence lists. Ear and hearing. 2012;33(1):112-7.

4) QuickSin Speech-in-Noise Test Version 1.3 User Manual.2001.Etymotic Research Inc.

5) Noble W, Jensen NS, Naylor G, Bhullar N, Akeroyd MA. A short form of the Speech, Spatial and Qualities of Hearing scale suitable for clinical use: the SSQ12. Int J Audiol. 2013;52(6):409-12.

6) Verheij E, Bezdjian A, Grolman W et al. A systematic review on complications of tissue preservation surgical techniques in percutaneous bone conduction hearing devices. Otology & Neurotology. 2016; 37:829-837.

7) International Organization for Standardization. ISO 14155:2011 Standard: Clinical investigation of medical devices for human subjects – Good clinical practice. 2011. Available at: https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-2:v1:en

8) World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 2013. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.

25 CHANGE HISTORY

Version	Change	Rationale
1.0	First draft of document	New Study
2.0	Changes to audiometric thresholds	To align with current FDA-approved indications for the Osia 2 Implant system
3.0	Changes throughout document to remove Cohort 2 (this includes updated inclusion criteria, endpoints, objectives, assessments, and analysis as a result of removal of Cohort 2)	Change to the study design was deemed necessary