Official Title: A pivotal, prospective, single-centre, randomized test order, crossover, open label study comparing the performance of a new sound processor - Baha 6 Max with unaided hearing and Baha 5 in adult subjects with conductive or mixed hearing loss.

NCT Number: NCT04559282

Document Date: 29 October 2020

Clinical Investigation Plan

Investigation Title:

A pivotal, prospective, single-centre, randomized test order, crossover, open label study comparing the performance of a new sound processor - Baha 6 Max with unaided hearing and Baha 5 in adult subjects with conductive or mixed hearing loss.

Short Title:	**Baha 6 Max Home test**
CIP Number:	**CBAS5779**
Version Number:	**4.0**
Date:	**29-OCT-2020**
Sponsor	**Cochlear Bone Anchored Solutions AB (CBAS)** **Konstruktionsvägen 14** **SE-435 33 Mölnlycke** **Sweden** **Phone: +46 31 792 44 00**

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 (1).

Manufacturer	Cochlear Bone Anchored Solutions AB Konstruktionsvägen 14 Mölnlycke 435 33 SWEDEN
Sponsor Organisations	Cochlear Bone Anchored Solutions AB Contact person: [redacted] Konstruktionsvägen 14 Mölnlycke 435 33 SWEDEN
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INVESTIGATOR AGREEMENT

Principal Investigator Approval and Declaration

By my signature below, I confirm my review and approval of this Clinical Investigational Plan (CIP).

I also confirm that I will strictly adhere to the requirements therein and undertake to ensure that all staff with delegated responsibilities in the conduct of this CIP have 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**
[redacted]	Principal Investigator
Signature	**Date**

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1 DEFINITIONS AND ABBREVIATIONS

Term	Description
ADE	Adverse Device Effect
AE	Adverse Event
CBAS	Cochlear Bone Anchored Solutions AB
CER	Clinical Evaluation Report
CHL	Conductive Hearing Loss
CIP	Clinical Investigation Plan
CRF	Case Report Form
DD	Device Deficiency
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GCP	Good Clinical Practices
IB	Investigator's Brochure
ICF	Informed Consent Form
IFU	Instructions for Use
IMD	Investigational Medical Device
MHL	Mixed Hearing Loss
PI	Principal Investigator
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SNR	Signal-to-noise Ratio
SOP	Standard Operating Procedure
SP	Sound Processor
SPL	Sound Pressure Level
SSD	Single-sided Sensorineural Deafness
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A pivotal, prospective, single-centre, randomized test order, crossover, open label study comparing the performance of a new sound processor - Baha 6 Max with unaided hearing and Baha 5 in adult subjects with conductive or mixed hearing loss.
Short title	Baha 6 Max Home test
Investigation number	CBAS5779
Name of investigational medical device(s)	The Baha 6 Max SP
Intended use of investigational medical device(s)	Intended use The Cochlear Baha System uses bone conduction to transmit sounds to the cochlea (inner ear) with the purpose of improving hearing. The Baha 6 Max SP is intended to be used as part of the Cochlear Baha System to pick up surrounding sound and transfer it to the skull bone via a Baha Implant, Baha Softband or Baha SoundArc and can be used unilaterally or bilaterally. Medical indications for use The Baha System is indicated for patients with conductive hearing loss, mixed hearing loss and single sided sensorineural deafness (SSD). The Baha 6 Max SP is indicated for patients with up to 55 dB SNHL. The regulatory status is pre-market.
Name and description of comparator device/product(s)	The comparator will be the Baha 5 SP. Intended use The Cochlear Baha System uses bone conduction to transmit sounds to the cochlea (inner ear) with the purpose of improving hearing. The Baha 5 SP is intended to be used as part of the Cochlear Baha System to pick up surrounding sound and transfer it to the skull bone via a Baha Implant, Baha Softband or Baha SoundArc and can be used unilaterally or bilaterally.

	Medical indications for use The Baha System is indicated for patients with conductive hearing loss, mixed hearing loss and single sided sensorineural deafness (SSD). The Baha 5 SP is indicated for patients with up to 45dB SNHL. The Baha 5 SP is a CE marked medical device.
Expected start date (first subject consented)	The start of the study has been delayed due to Covid-19 pandemic. New estimated start date beginning of September 2020.
Expected enrolment period	6 weeks
Expected duration per subject	14 days +/- 4 days
Expected total duration of the clinical investigation	8 weeks
Number of subjects planned	16
Number of investigational sites planned	One site
Inclusion criteria	• Adult subject (18-<70 years of age) • At least 12 months experience from using a Baha Connect system (percutaneous Baha) • Subject with a conductive or mild to moderate mixed hearing loss. that would benefit from improved hearing from bone conduction device as judged by the research audiologist • Willing and able to provide written informed consent
Exclusion criteria	• Signs of infection around the implant site • Unable to follow investigational procedures • Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator

	• Investigator site personnel directly affiliated with this investigation and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling. • Cochlear employees • Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device.

Objectives and Endpoints	
Primary Objectives	**Primary Endpoints**
To compare hearing performance of speech in noise between Baha 6 Max and the unaided hearing (superiority). To compare the preference of device between Baha 6 Max SP and Baha 5 SP	Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] Preference of device
Secondary Objective	**Secondary Endpoint**

To compare hearing performance between Baha 6 Max and Baha 5 SP in a home/normal hearing environment	• Diary
	  ○ Daily use of the SP (hours)
	  ○ Change of battery
	  ○ Switch to their own SP and reason for change

To compare hearing performance between Baha 6 Max and Baha 5 SP.	• Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] • Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0 9.0 and 10.0 kHz] • Speech in quiet [% correctly perceived words at 65dB SPL] • Evaluation of sound quality and listening effort through sound clips
To compare hearing performance between Baha 6 Max and unaided.	• Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0, 9.0 and 10.0 kHz] • Speech in quiet [% correctly perceived words at 65dB SPL]

Safety Objective	Safety Outcome measures
Adverse events	Information will be collected from Visit 1 and onwards.
Device deficiency	Information will be collected from Visit 1 and onwards.

3 SCHEDULE OF EVENTS

Visit/Type of visit	Visit 1	Visit 2	Visit 3	Extra Visit
Timing of Investigation	**Day 0**	**Day 7**	**Day 14**	
Visit window (±)	**± 0 Day**	**± 2 days**	**± 2 days**	
Baseline information				
Written informed consent	X			
Demographics	X			
Eligibility	X			
Hearing history incl. audiogram	X			
Device history	X			
Medical history	X			
Fitting of SP to be tested	First randomised device to bring home	Second randomised device to bring home	Re-fitting	Current device
Feedback test	X	X	X[a]	X[b]
BC-Direct	X	X	X[a]	X[b]
Fine tuning	X[b]	X[b]	X[b]	X[b]
Choice of snap coupling	X[c]	X[c]		X[c]
Test procedures in sound booth	Aided First device	Aided Second device	Unaided	
Blocking incl. verification of contralateral ear	X	X	X	
Adaptive speech in noise (Matrix)	X	X	X	
Threshold audiometry in sound-field	X	X	X	
Speech in quiet at 65 dB SPL	X	X	X	
Subjective evaluation by research subject based on home test		First device	Second device	
Hand-out Diary	X[d]	X[d]		
Review Diary		X	X	
Preference of device			X	
Subjective evaluation by research subject based on sound clips (blinded evaluation)			First and second device	
Evaluation of sound quality and listening effort through sound clips			X[e]	
Safety evaluation				
Adverse Events (AEs)	X	X	X	
Device Deficiencies (DDs)	X	X	X	

[a] *Reprogram the first randomised device (Baha 5 SP or Baha 6 Max)*
[b] *Should be performed, if needed*
[c] *Only applicable to Baha 6 Max.*
[d] *Instruction on how to complete Diary*
[e] *Randomised order*

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

Developed in the late 1970's, Bone Conduction hearing implant systems are a well-established treatment modality that has proven to be a safe and effective way of providing hearing in patients with Conductive hearing loss (CHL), Mixed Hearing Loss (MHL) or Single-sided Sensorineural Deafness (SSD.

The Cochlear Baha System uses bone conduction to transmit sounds to the cochlea (inner ear) with the purpose of improving hearing.

The Baha Connect system (figure 1) consists of a titanium implant, which connects to a SP (SP) via a skin-penetrating (percutaneous) abutment. The SP (1) transforms sound into vibrations that are transmitted via the abutment (2) and osseointegrated titanium fixture (3) to the skull bone and onwards to the cochlea.

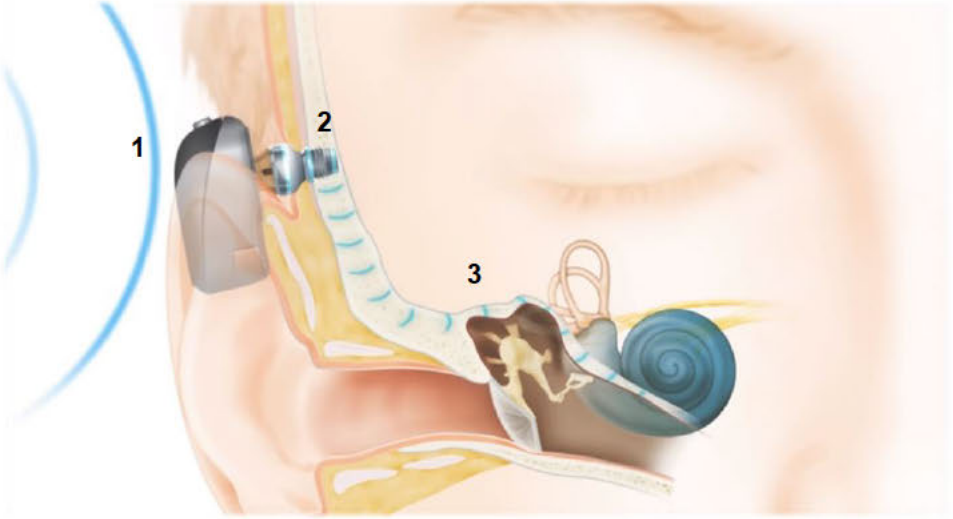


Figure 1. Schematic presentation of the Baha Connect System

The new SP - the Baha 6 Max - is intended to be used as part of the Cochlear Baha System to pick up surrounding sound and transfer it to the skull bone via a Baha Implant, Baha Softband or Baha SoundArc and can be used unilaterally or bilaterally. The Baha 6 Max SP is indicated for patients with up to 55 dB SNHL (2).

4.2 Findings of Previous Nonclinical and Clinical Studies

4.2.1 Nonclinical Data

Results from technical verification and validation activities are described in the Investigator's Brochure (3).

4.2.2 Clinical Data

The previously released and comparator device Baha 5 SP has similar characteristics as Baha 6 Max SP (3). The clinical data for Baha 5 SP appraised and analysed from systematic literature review and exploratory clinical investigations demonstrate good objective hearing outcomes, with consistently improved sound-field thresholds (PTA4, mean of 0.5, 1, 2 and 4 kHz), speech recognition in quiet and in noise as compared to the unaided condition. There are no high risks relating to the use of the Baha SPs or accessories (section 3 in IB, (3)).

5 MEDICAL DEVICE INFORMATION

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

The Baha 6 Max SP is a fully programmable, head-worn, SP with support for direct audio, data streaming and wireless connection to Cochlear Wireless Accessories, among other features. It has been developed to meet the needs of patients with CHL, MHL or SSD (3).

Figure 2. The Baha 6 Max SP

The Baha 6 Max SP receives sound from its two microphones. Digital audio can be received through wireless streaming from the wireless accessories or from a compatible iPhone.

The SP processes the received information and generates a mechanical signal, i.e. a force output that is transferred to the skull of the patient via the implant system. The vibration is generated by an electromagnetic actuator (3).

The SP contains signal processing features to enhance the patient's hearing experience. These are further described in the IB (section 1.2, (3)).

The material used in the Baha 6 Max SP is described in the Investigator Brochure (section 1.2, table 2, (3)).

Research subject that will participate in the investigation are experienced SP users. They will be provided with an Instructions for Use (IFU) (4).

The manufacturer of Baha 6 Max SP is CBAS.

5.2 Identity and Description of the Comparator

The Cochlear Baha 5 SP is the predecessor to Baha 6 Max SP.

The Baha 5 SP uses bone conduction to transmit sounds to the cochlea (inner ear). It is indicated for people with conductive hearing loss, mixed hearing loss and single sided sensorineural deafness (SSD). Furthermore, it is indicated for bilateral and paediatric recipients. Fitting range up to 45 dB SNHL (2).

Baha 5 SP is CE-marked.

Figure 3. The Baha 5 SP

The manufacturer of Baha 5 SP is CBAS.

5.3 Interfaces

An audiologist uses programming software—Fitting Software—to modify hearing profiles in order to provide comfortable and usable gain for the sound processor for each user (Baha Connect System recipient). Communication between the computer-based software and the sound processor is achieved using a Noahlink Wireless programming unit. Baha Fitting Software is used in clinic by audiologists or similar trained hearing healthcare professionals e.g. research audiologists (section 1.3 in IB, (3)).

6 OBJECTIVES AND ENDPOINTS

Primary Objectives	Primary Endpoints
To compare hearing performance of speech in noise between Baha 6 Max SP and the unaided hearing (superiority). To compare the preference of device between Baha 6 Max SP and Baha 5 SP	Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] Preference of device
Secondary Objectives	**Secondary Endpoints**
To compare hearing performance between Baha 6 Max SP and Baha 5 SP in a home/normal environment hearing environment	• Diary o Daily use of the SP (hours) o Change of battery o Switch to their own SP and reason for change
To compare hearing performance between Baha 6 Max SP and Baha 5 SP.	• Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] • Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0, 9.0 and 10.0 kHz] • Speech in quiet [% correctly perceived words at 65dB SPL] • Evaluation of sound quality and listening effort through sound clips
To compare hearing performance between Baha 6 Max SP and unaided.	• Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0 and 8.0 kHz] • Speech in quiet [% correctly perceived words at 65dB SPL]
Safety Objective	**Safety Outcome measures**
Adverse events (AEs)	Information will be collected from Visit 1 and onwards.
Device deficiency (DDs)	Information will be collected from Visit 1 and onwards.

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

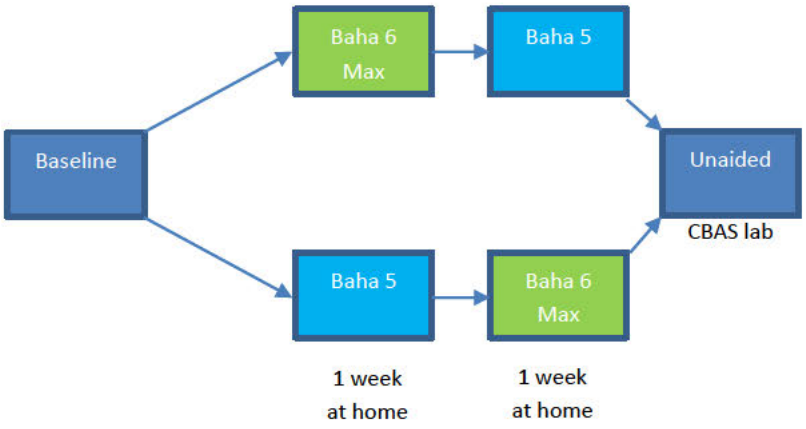


Figure 4. Schematic for the investigation

This investigation is a pivotal, prospective, single-centre, randomized test order, cross-over, open label investigation comparing the performance of a new SP - Baha 6 Max SP with unaided hearing and Baha 5 SP in adult subjects with conductive or mixed hearing loss.

The evaluation of sound quality and listening effort through sound clips at visit 3 will be performed single-blinded, i.e. the test subject will not know if Baha 6 Max SP or Baha 5 SP is connected to the abutment.

The subjects include men and women aged 18 or older who are currently using the Baha Connect System (percutaneous Baha). Subjects will be screened, and 16 eligible subjects will be enrolled in the clinical investigation. Eligible subjects will be randomly assigned to one of two investigational arms using a 1:1 randomisation ratio. Subjects will be randomised either to first test the Baha 6 Max SP and thereafter Baha 5 SP or Baha 5 SP followed by Baha 6 Max SP.

After signing the informed consent, subjects will attend scheduled study visits over a three-week period to be assessed as described in the CIP Schedule of Events (Section 3). At study visits, subjects will undergo hearing assessments and safety assessments.

The first primary endpoint is to determine the hearing performance of Baha 6 Max SP in comparison with unaided hearing and the second primary endpoint is the comparison of preference between the devices. The second primary objective is to compare the hearing performance between Baha 6 Max SP and Baha 5 SP when it comes to subject preference.

Safety will be assessed by recording and summarising all AEs/ADEs and DDs. All subjects will attend an End-of-Study visit at the time they complete the investigation.

No data monitoring committee will be used for this clinical investigation.

After the investigation a subject will continue to use the SP currently prescribed to him/her.

7.1.1 Design Rationale

The primary purpose with this investigation is to test the Baha 6 Max SP versus unaided hearing in order to achieve regulatory approval and to investigate which device (Baha 6 Max versus Baha 5) the subjects prefer.

The second primary objective is to compare hearing performance between Baha 6 Max SP and Baha 5 SP in a home (normal) hearing environment. The subjects will test the two SPs during a week at home in a cross-over design (randomised test order). Based on their experiences with the SPs the subject will be asked which of them they prefer. Because all subjects are prescribed and used to amplified sound through bone conduction, one weeks testing at home is regarded as sufficient time to evaluate the performance of a SP. The investigation must be performed in an open fashion since it is not possible to blind the investigation due to differences in design.

After fitting of the test device several listening tests (adaptive speech in noise, thresholds audiometry and speech in quiet) will be performed in a sound booth.

The evaluation of sound quality and listening effort through sound clips (visit 3) will be performed in a blinded fashion, i.e. the subject will not know which SP that is tested. The test order will be randomised

7.2 Subjects

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

7.2.1 Inclusion Criteria

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

1. Adult subject (18-<70 years of age)
2. At least 12 months experience from using a Baha Connect system (percutaneous Baha)
3. Subject with a conductive or mild to moderate mixed hearing loss. that would benefit from improved hearing from bone conduction devise as judged by the research audiologist
4. Willing and able to provide written informed consent

7.2.2 Exclusion Criteria

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

1. Signs of infection around the implant site
2. Unable to follow investigational procedures
3. Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator
4. Investigator site personnel directly affiliated with this investigation and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.

5. Cochlear employees
6. Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device.

7.2.3 Number of Subjects Required

In order to meet the sample sizes calculations for both primary analyses, 16 subjects will be included.

As this is an internal Cochlear investigation, patients will be recruited until the number of required patients are enrolled. Hence, no dropouts are expected.

7.2.4 Vulnerable Populations

No applicable

7.2.5 Enrolment & Study Duration

The following subject status definitions apply:

Screened: *A consented subject who 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: First use of the IMD or comparator following completion of screening activities and confirmation of eligibility

The expected duration of each subject's participation in the clinical investigation is 3 weeks, from the time of informed consent to the End of Study visit.

The enrolment period for the clinical investigation is anticipated to be 6 weeks from the time of first subject consent to enrolment of the last subject.

The anticipated total duration of the clinical investigation is therefore 8-9 weeks.

Clinical Investigation completion is last subject last visit. In the event of an ongoing SAEs/SADEs at the time of this last visit, the clinical investigation completion will be extended for a further 30 days, or until resolution or stabilisation of the event, whichever comes first.

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 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 IMD 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 must be documented.

Enrolled subjects who are withdrawn/discontinued will not be replaced. Randomisation Procedures

The test order between the two SPs will be randomised based on a computer-generated randomisation schedule prepared by the Sponsor.

7.2.6.1 Blinding Procedures

Blinding of the SPs during the home test is not possible due to the differences in design.

When performing the subjective evaluation of sound clips the subjects will be blinded to which SP (Baha 6 Max SP or Baha 5 SP) currently tested, i.e. single-blind. This is possible since the investigator will place the SP on the abutment without showing the subject.

7.2.7 Post-investigation Medical Care

After the investigation a subject will continue to use the SP currently prescribed to him/her.

7.3 Performance Evaluations and Procedures

7.3.1 Eligibility Evaluations and Procedures

Demographics

The following demographic data will be recorded at Screening and Baseline:

- Age collected as date of birth (month and year)
- Gender

Hearing history

During Screening and Baseline a number of baseline characteristics will be recorded:

- Type of hearing loss
- Etiology of hearing loss: (chronic) infection, tumor, trauma, malformation, otosclerosis, other
- Current hearing aid
- Treatment ear

Audiogram

Unaided audiometric threshold measures (including both air- and bone conduction thresholds) should demonstrate whether the subject has a conductive or mild to moderate mixed hearing loss and meets the audiological inclusion criteria.

An existing audiogram may be used as long as it has been completed during the last twelve months and contains all the required relevant frequencies. Frequencies required for air and bone conduction thresholds are 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000Hz.

If an audiogram is older than 12 months or does not contain the required frequencies, a new audiogram shall be performed at Screening/Baseline. Frequencies required for air and bone conduction thresholds are 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000Hz. Contralateral masking should be used if needed. The site staff shall always measure both the unmasked thresholds, as well as and the masked thresholds, if applicable.

7.3.2 Post-Enrolment Evaluations and Procedures

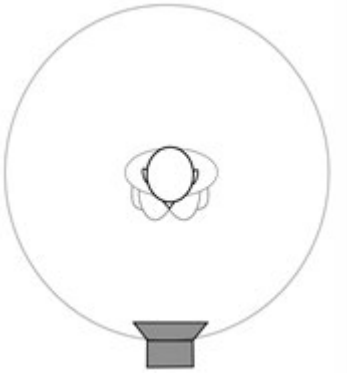
7.3.3 Adaptive Speech recognition in noise (Matrix test)

The purpose of this test is to establish the test subject's ability to recognise speech in the presence of background noise. The adaptive speech test in noise shall be conducted using validated lists of phonetically balanced sentences, with speech presented in sound-field from the front (0 degrees azimuth) and noise will also be presented from the front (figure 4). The noise shall be kept constant at 65 dB SPL, and the speech shall be adapted stepwise according to the software used to establish the speech-to-noise ratio (SNR) providing a 50% level of understanding.

Software and speech material to be used is the Matrix test in language specific versions as applicable.

The test shall be performed with the non-test ear blocked (in case of normal or near-normal hearing or a large asymmetry with the non-test ear having significantly better hearing thresholds).

The speakers should be at the height of the test subjects head and more than 1 metre away from the test subject. There should preferably be more than 1 metre of free space around the test subject in all directions. This is in accordance with the current standard.



FRONT

Figure 5: Speech in noise speaker position

At Visit 1 and 2, the speech in noise test will be performed for the aided situation with Baha 6 Max SP or Baha 5 SP depending on the randomisation order.

At visit 3 the test will be performed unaided.

7.3.4 Sound-field threshold

The purpose of this test is to establish the hearing thresholds in sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0 9.0 and 10.0 kHz] through a speaker in front position (0 degrees azimuth) according to the so-called ascending or modified Hughson-Westlake method (Figure 10). The test shall be performed with the non-test ear blocked (in case of normal or near-normal hearing or a large asymmetry with the non-test ear having significantly better hearing thresholds). The signal to be used should be warble tones.

At Visit 1 and 2, the sound-field thresholds will be measured in the aided situation with Baha 6 Max SP or Baha 5 SP depending on the randomisation order.

At visit 3 the test will be performed unaided.

7.3.5 Speech recognition in quiet

The purpose of this test is to establish the test subject’s word recognition score in quiet. The speech test in quiet shall be performed using phonetically balanced words presented in sound-field through a speaker from the front (0 degrees azimuth) (figure 10). The test material shall be monosyllabic words and presented at 65 dB sound pressure level (SPL) and scores shall be recorded as % correct words. The test shall be performed with the non-test ear blocked (in case of normal or near-normal hearing or a large asymmetry with the non-test ear having significantly better hearing thresholds).

At Visit 1 and 2, the speech recognition in quiet test will be performed for the aided situation with Baha 6 Max SP or Baha 5 SP depending on the randomisation order.

At visit 3 the test will be performed unaided.

7.3.6 Sound scenarios

Subjective rating of sound, i.e. loudness, sound quality, speech understanding, own voice, artefacts and feedback after listening to sound clips in the following sound scenarios:

- Female voice in a noisy restaurant environment at 65 dBSPL
- Music at 70 dBSPL

7.3.7 Diary

Subject will complete daily the diary which covers the following items:

- Daily use of the SP (hours)
- Change of battery
- Switch to their own SP and reason for change

7.4 Safety Evaluations and Procedures

The risks and anticipated ADEs for Baha 6 Max SP or Baha 5 SP, as identified in Sections 7.2 and 8.3 of the CIP, will be assessed in the clinical investigation via reporting of all AEs/ADEs from the time of first subject first visit until last subject last visit.

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

7.5 Equipment Used for Evaluation of Performance and Safety

All tests shall be performed in the sound insulated room at CBAS. Equipment used for audiological testing will be calibrated in accordance with CBAS internal procedures before initiation of the investigation. No changes to the setup will be done during the investigation.

7.6 Sponsor Role in Conduct of the Clinical Investigation

The investigation will be conducted by audiologist employed by CBAS and the investigation will be conducted at CBAS facilities.

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

8.1 Anticipated Clinical Benefits

There are no anticipated clinical benefits for the research subjects as they only test the investigational devices for one week in their everyday listening environment and in a laboratory setting. After study completion, the subjects will use the SP currently prescribed to him/her by a licensed audiologist within the regular healthcare system.

8.2 Anticipated Adverse Device Effects

The complete Hazard Analysis for Baha 6 Max SP can be viewed in appendix B in IB, (3).

8.3 Risks Associated with Participation in the Clinical Investigation

Baha Connect System has been thoroughly examined in terms of clinical safety and in a comprehensive analysis of available pre- and post-market clinical and non-clinical data relevant to the intended purpose of the devices in question, the clinical evaluation concludes that the Baha Connect System is safe and performs as intended, with a positive benefit-risk profile shown for the different target groups and medical indications. Although four (4) residual high risks were identified, for the Baha Connect System, none of them are associated with the sound processor.

Importantly, for this evaluation of the Baha 6 Max SP, none of the 'high' residual risks for the Baha Connect system relates to the SP (section 4.3 in IB, (3)).

The updated risk assessment for Baha 6 Max SP is presented in table 1.

Table 1. Summary of Medium/High risks for Baha 6 Max SP

Harm	Hazard Description	Severity of harm	Probability of Occurrence of Harm	Residual risk
Infection	Microbiological cross contamination for user or personnel due to poor cleaning or cut injury (various causes)	Serious	Improbable	Medium
Adverse tissue reaction	Allergic reactions of user or assembly technicians i.e. research audiologists	Serious	Improbable/ remote	Medium
Life threatening injury	Device causes sparks in flammable or explosive environments leads to explosion	Catastrophic	Improbable	Medium
Permanent tissue or neural damage	Fitting the device results in too loud sound	Critical	Improbable	Medium
Permanent tissue or neural damage	Skull fracture due to impact force on the sound processor.	Critical	Improbable	Medium
Suffocation	Child swallows battery or device leading to suffocation	Catastrophic	Improbable	Medium

Suffocation	Safety line entangles around wearer's neck.	Catastrophic	Improbable	Medium
Surgical intervention and/or implantable device replacement	Device sits too tight on abutment causes loss of osseointegration	Critical	Improbable	Medium

8.4 Risk Mitigation

Control and mitigation of risks for Baha 6 Max SP are detailed in the Hazards Analysis in the IB. All risk reduction measures implemented as design controls have been verified to be effective (appendix B in IB, (3)).

Due to Covid-19 more subjects are in working age and as a possible result to that more subjects are bilateral sound processor users than anticipated. Because of this approximately 6 IMD will need to be reused during the investigation. To mitigate cross contamination between subjects the devices will be cleaned according to a validated cleaning procedure for Acoustics products (5) (6) and a Cleaning and disinfection record (7) will document which IMD that has been cleaned.

8.5 Risk-to-Benefit Rationale

The Baha 6 Max SP is the successor of the Baha 5 SP, which has been on the market for five years. Baha Connect System has been thoroughly examined in terms of clinical safety and in a comprehensive analysis of available pre- and post-market clinical and non-clinical data relevant to the intended purpose of the devices in question, the clinical evaluation concludes that the Baha Connect System is safe and performs as intended, with a positive benefit-risk profile shown for the different target groups and medical indications. Although four (4) residual high risks were identified, these were deemed acceptable given the benefits provided by the system to the patients (section 4.1 in IB, (3)).

Due to the Covid-19 pandemic, a majority of the employees at CBAS are currently working from home and a limit of 25% (N = 60) is allowed to work in the CBAS facility. Moreover, all employees at CBAS have undergone training on work safety guidelines and must comply with the following guidelines should they chose to work in the office building. In order to protect oneself and everyone else at work, the CBAS guidelines state:

- *Stay at home if you have cold and/or flu symptoms*
- *Wash your hands often and thoroughly*
- *Refrain from touching your face, nose and eyes*
- *Cover your mouth and nose with a tissue when you cough/sneeze or cough/sneeze into your elbow*

- *Always keep a distance of 1.5 meters between yourself and your colleagues*
- *No handshaking*

Do not come into the office if you have any of the following symptoms (based on the list of symptoms provided by The Public Health Agency, Folkhälsomyndigheten, Sweden):

- *Cough*
- *Fever*
- *Difficulty breathing*
- *Runny nose/blocked nose*
- *Sore throat*
- *Headache*
- *Nausea*
- *Muscle and joint pain*
- *Loss of taste/smell*

Everyone must be symptom-free in order to enter the facility. We ask you to reflect upon your health status each day and confirm that you are symptom-free before entering the facility in order to protect each other. When entering the facility, you need to:

1. *Sign your name in the ledger to confirm that you are Covid-19 symptom free*
2. *Sanitize your hands at the hand sanitizer station (pump the bottle three times)*
3. *Walk directly to your workstation*

To further decrease the risk of infection, the CBAS guidelines also state that colleagues should have a social distance when sharing cars for lunch, avoid rush hour if using public transport to/from the workplace, meeting rooms can only be used with a limited number of participants (depending on the size of the meeting room) and meeting owners are responsible for sanitizing used equipment when the meeting ends prior to leaving the room. When working in labs and/or sound booths, all equipment used must be sanitized before leaving the lab/sound booth and face masks must be used if two or more employees are in the lab at the same time. The following guidelines for the use of face masks are:

- *Face masks should cover both your nose and mouth*
- *Do not touch the face mask while being worn to avoid contamination*
- *When leaving the room for a longer period throw away your face mask and use a new one when reentering*
- *When removing a face mask, you should use the band/ties to remove it (i.e. do not touch the material covering your mouth/nose)*

Currently, visitors are not allowed into the CBAS facility. Exceptions must be approved by a member of the executive team. Hosts receiving approved visitors must ask visitors to confirm they do not have any Covid-19 symptoms. The host is also responsible for ensuring their visitors upholds the measures set out in these guidelines.

For study participants, most of the above listed guidelines will apply such as being symptom-free when asked about interest in study participation during the recruitment process and in all study visits, sanitize their hands when entering the CBAS facility, keeping a social distance of 1.5 meters to all employees in the facility, no handshaking and covering mouth/nose when coughing/sneezing. However, it should be noted that some exceptions to the above listed guidelines must apply. For example, when entering the CBAS facility, none of the study participants will have to sign their name on a ledger (in order to certify that they are symptom-free) to protect their privacy as study participants. A social distance of 1.5 meters between the clinical research audiologist and the test subject will be kept as much as possible during all visits. An exception is during implant inspection as the audiologist has to rule out infection around the implant area before the start of the study. During the implant inspection, the audiologist will use disposable plastic gloves and a face shield visor. The face shield visor will be worn by the audiologist during the whole session for each study visit. The primary reason for using a face shield visor and not face masks during study visits or in the lab is because face masks make lipreading impossible. Hard of hearing people rely highly on facial expressions and visual cues in order to compensate for missing verbal information. Thus, it is of crucial importance that we ensure all test subjects understand all information provided to them during the study, both for their own safety and the validity of the study results.

To further minimize the risk of infection for the participant and CBAS employees, the participants will either take their own car to the CBAS facility or we will book a taxi where they will be placed in the backseat (i.e. distance to the driver). Public transport to/from the CBAS facility will not be allowed. Between each visit, the audiologist will sanitize all equipment used such as technical equipment, chairs, tables, door handles, etc.

It is essential for CBAS to conduct the planned study in due time because the previous generation of Baha Sound Processor (i.e. the Baha 5 SP) was introduced in 2015 and the regulatory approved product lifetime for this device is five years. Thus, CBAS prefer to certify the investigational device and enable patients to benefit from all the technical improvements and new features introduced in the new generation of Baha, i.e. the Baha 6 Max sound processor. For more information about technical improvements and new features in Baha 6 Max, see section *1.2 The investigational medical device* in the Investigator's Brochure.

In summary, a wide range of measures to prevent Covid-19 transmission have already been applied for all employees at the CBAS facility and will be applied to all study participants to minimize the risk of infection. Face shield visors instead of face masks will be used during all visits by the audiologist as we believe that face masks will cause communication difficulties which in turn will negatively affect the safety of the participants and the validity of the study results. We believe that the benefits of performing the current study (with all preventive measures taken for both employees and study participant) outweigh the risks as this study will enable the next generation Baha sound processor to

be released to the market in due time and with that give current and future Baha users access to all the technical benefits that comes with it.

9 STATISTICAL CONSIDERATIONS

9.1 General Statistical Considerations

The investigation will have two primary analyses, one regarding Adaptive speech in noise between Baha 6 Max SP and unaided hearing (alpha = 0.005) and one regarding preference between Baha 6 Max SP and Baha 5 SP (alpha = 0.045). These endpoints will be evaluated using the decision rules of the Holm's test. (Ref NEJM2). With these procedures we will have a total type I error <0.05.

For the comparison between the Baha 6 Max SP and unaided the design don't take care of period effect so the statistical analyses will be paired. For the comparison between Baha 6 Max SP and Baha 5 SP a cross over design was applied and the statistical analyses will be adjusted for period effect.

The main results for all outcome variables are the estimate of mean differences with 95% confidence interval (CI) with a descriptive p-value. The p-value will only have a confirmatory value for the two primary analyses.

For comparison between the Baha 6 Max SP and unaided Fisher's non-parametric permutation test for paired observations will be used for continuous variables and Sign test for dichotomous variables and ordered categorical variables.

For the comparison between Baha 6 Max SP and Baha 5 SP the following period adjusted analysis should be performed for continuous variables: For each subject take the difference between the measurement in second period and the measurement in first period. Then analyse these differences between the subjects randomised to Baha 6 Max SP in the first period and the subjects randomised to Baha 5 SP in the first period with Fisher's two-sided non-parametric permutation test. The Fisher's permutation test is preferable because it is non-parametric and gives consistent 95% CI.

For the comparison between Baha 6 Max SP and Baha 5 SP the following period adjusted analysis should be performed for dichotomous and ordered categorical variables: For each subject take the difference as, improved no change and worsened, between the measurement in second period and the measurement in first period. Then analyse these ordered categorical differences between the subjects randomised to Baha 6 Max SP in the first period and the subjects randomised to Baha 5 SP in the first period with Mantel-Haenszel chi-square test.

For comparison of preference of device between Baha 6 Max SP and Baha 5 SP the Sign test will be used.

The distribution of continuous variables will be given as mean, standard deviation, median, Q1, Q3, minimum and maximum and of categorical variables as numbers and percentages.

If a subject completes the cross over part but not the final visit, he will be included in the comparison between Baha 6 Max SP and Baha 5 SP but not in the comparison Baha 6 Max SP vs unaided in FAS.

The investigation will be completed when there are as many available subjects that are needed in the primary analyses.

The main analyses will be on the full analysis set (FAS) and complementary analyses on the Per protocol population. No imputation of missing data will be performed.

9.2 Endpoints

- Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding]
- Preference of device. Only Baha 6 Max SP and Baha 5 SP.
- Diary. Only Baha 6 Max SP and Baha 5 SP.
  - Daily use of sound processors (hours)
  - Change of battery
  - Switch to their own sound processor and the reason for change
- Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0 9.0 and 10.0 kHz]
- Speech in quiet [% correctly perceived words at 65dB SPL]
- Evaluation of sound quality and listening effort through sound clips. Only Baha 6 Max SP and Baha 5 SP.

9.2.1 Primary Endpoints

- Primary endpoint for comparison between Baha 6 Max SP and unaided.
  - Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding]
- Primary endpoint for comparison between Baha 6 Max SP and Baha 5 SP.
  - Preference of device.

9.2.2 Secondary Endpoints

- Daily use of sound processors (hours) from Diary, Only Baha 6 Max SP vs Baha 5 SP
- Change of battery from Diary, Only Baha 6 Max SP vs Baha 5 SP
- Switch to their own sound processor and the reason for change from Diary

, Only Baha 6 Max SP vs Baha 5 SP

- Adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] Baha 6 Max SP and Baha 5 SP
- Thresholds audiometry, sound-field [0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0 9.0 and 10.0 kHz]

- Speech in quiet [% correctly perceived words at 65dB SPL]
- Evaluation of sound quality and listening effort through sound clips. Only Baha 6 Max SP and Baha 5 SP.

9.3 Hypotheses

9.3.1 Primary Hypothesis

The first primary efficacy analysis is the comparison regarding adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] between Baha 6 Max SP and unaided using a two-sided Fisher's non-parametric permutation test for paired observations on significance level 0.005.

H_0: $\mu_{\text{Baha 6 Max SP}} = \mu_{\text{unaided}}$
H_1: $\mu_{\text{Baha 6 Max SP}} > \mu_{\text{unaided}}$ or $\mu_{\text{Baha 6 SP}} < \mu_{\text{unaided}}$

The second primary efficacy analysis is the comparison regarding preference of device between Baha 6 Max SP and unaided using a two-sided Sign test on significance level 0.045.

H_0 : Probability preference of Baha 6 Max SP before Baha 5 SP =0.5, given preferred any.
H_1 : Probability preference of Baha 6 Max SP before Baha 5 SP >0.5, given preferred any or Probability preference of Baha 6 Max SP before Baha 5 SP <0.5, given preferred any.

9.4 Sample Size Determination

First primary analysis: Baha 6 Max SP vs unaided regard Adaptive speech in noise

Assuming an individual mean difference (aided Baha 6 Max SP minus unaided) in speech recognition in noise of 16 dB SNR with a standard deviation (SD) of 12.5 (Busch et al, 2015), a total sample of 15 eligible subjects are required to provide 90% power to reject the null hypothesis for the statistical test for the primary objective (change in dB SNR) using a two sided, alpha 0.005, with Two-sided Fisher's non-parametric permutation test for paired observations. As this is an internal Cochlear investigation, patients will be recruited until the number of required patients are obtained. Hence, no dropouts are expected (8).

Second primary analysis: Baha 6 Max SP vs Baha 5 SP regarding preference of device.

Assuming that 86% prefer Baha 6 Max SP, then 16 subjects are needed for 80% power with two-sided Sign test on significance level 0.045.

In order to satisfy both sample sizes for the primary analyses 16 subjects will be randomised into the investigation.

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9.5 Analysis Populations

9.5.1 Full Analysis Set

The Full Analysis Set will consist of randomized subjects that have at least one measurement on two of the periods Baha 6 Max SP, Baha 5 SP and unaided.

9.5.2 Per Protocol Population

The Per protocol population will consist of all randomized patients that have measurements on all primary and secondary variables on all three periods and have no major protocol violations.

9.6 Primary Endpoint Analyses

The first primary endpoint analysis will be the comparison of adaptive speech in noise [signal-to-noise ratio, 50% speech understanding] between the Baha 6 Max SP and unaided with two-sided Fisher's non-parametric permutation test for paired observations on significance level 0.005 on the FAS population. Mean difference with 99.5% confidence interval will be given together with the distribution of the difference.

The second primary endpoint analysis will be the comparison between Baha 6 Max SP and Baha 5 SP regarding preference of device with two-sided Sign test on significance level. Proportion of preferences for Baha 6 Max SP with exact 95 % CI will be calculated.

If one of the two primary efficacy analyses are significant but not the other, the other can be retested at the 5% significance level according to the decision rule of the Holms test (9).

9.7 Secondary Endpoint Analyses

All the secondary endpoints in section 8.2.2 will be analysed according to the statistical methods given in section 8.1 General Statistical Considerations on both the FAS population and the Per Protocol population. The two primary efficacy analyses will also be performed on the Per Protocol population

9.8 Safety Analyses

The Adverse Event will be analysed descriptively for the Safety population.

Adverse Events and Serious Adverse Events will be coded with the MeDRA dictionary and tabulated by Preferred Term-code and System Organ Class-code and treatment.

9.9 Demographics and Baseline Characteristics

Demographics and baseline characteristic will be descriptively summarised

9.10 Interim Analyses

N/A

9.11. Statistical Analysis Plan

A statistical analysis plan (SAP) with detailed statistical analyses specified for all variables will be written and signed off before the database lock.

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). 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 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, or
- Chronic disease.

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

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.

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 Investigator's Brochure

NOTE: An anticipated serious adverse device effect is an effect, which by its nature, incidence, severity, or outcome has been identified in the Investigator's Brochure.

11.1.6 Adverse Events of Special Interest

N/A

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 enquire about AEs at investigation visits.

AEs will be recorded from the time of first use/contact with the IMD and/or comparator. AE recording will continue for each subject until completion of their End of Study visit. Ongoing SAEs and SADEs will be followed for 30 days, or until resolution or stabilisation of the event, whichever comes first.

Source notes should indicate the evaluation for AEs, even if 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 IMD and/or comparator 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.

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:

Table 3. Intensity of event.

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 IMD and/or comparator product will be considered and investigated. The causal relationship to the IMD and/or comparator is to be assessed by the Investigator (or medically qualified delegate) and should be assessed using the following classifications:

Table 4. Potential causal relationship of event.

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 and the definition provided in section 11.1.3.

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 8.2 and 8.3 of this CIP and/or the Investigator's Brochure> are anticipated ADEs.

Table 5. Assessment of Expectedness.

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. Source notes should indicate the evaluation for DDs, even if 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;

a) suitable action had not been taken,

b) intervention had not been made, or,

c) circumstances had been less fortunate

All DDs will be documented in the source notes and the DD page of the CRF.

11.4 Reporting Responsibilities

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

11.4.1 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 during the same working day.

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 11.2.2 '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.

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. SAEs will be reported in accordance with MEDDEV 2.7/3, revision 3, May 2015 (10):

The sponsor must report to the NCAs where the clinical investigation has commenced:
- for all reportable events as described in section 4 which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons [11] or a new finding to it: immediately, but not later than 2 calendar days after awareness by sponsor of a new reportable event or of new information in relation with an already reported event.

- any other reportable events as described in section 4 or a new finding/update to it: immediately, but not later than 7 calendar days following the date of awareness by the sponsor of the new reportable event or of new information in relation with an already reported event.

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 SAEs, unanticipated ADEs, DDs that could have led to an SADE.

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

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

11.5 Independent Data Monitoring Committee

Not applicable.

12 DEVICE ACCOUNTABILITY

Supply of investigational medical devices will be recorded using the Sponsor Device Tracking Form (1295388). Investigational medical device(s) will be quarantined at the investigational site and clearly labelled to identify exclusively for use in a clinical investigation.

Subject level device supply will be tracked in the CRF.

13 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 24 hours from the date of the emergency.

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, 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: First use of the IMD or comparator following completion of screening activities and confirmation of eligibility
- Withdrawn: Enrolled subjects who withdraw or are withdrawn by the Investigator or Sponsor before the expected End of Study visit. Withdrawn subjects may continue in safety follow up until their scheduled 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.

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.

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 favourable 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. 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

17.1 Reporting to regulatory authority

If this investigation is suspended or terminated prematurely, the Swedish Medicines Agency shall be informed within 24 hours whether it is for safety reasons that the trial is terminated or cancelled, otherwise within 15 calendar days. When a trial is completed according to plan, the Swedish Medicines Agency must be informed within 15 calendar days after the trial has ended (last subject last visit).

18 AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

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, 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.

The investigator must retain study-related records for a period of at least 15 years after completion of the investigation or after the last device was placed on the market, if the IMD has market authorisation.

20 PUBLICATION POLICY

This clinical investigation will be prospectively registered at a public clinical trial registry, i.e. 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 (8) (9) 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 (11), International Standard ISO 14155 Clinical investigation of medical devices for human subjects - Good Clinical Practice (1), 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 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 (SOP) to ensure that clinical study procedures and documentation are consistently conducted and compliant with the ISO 14155 Standard, Good Clinical Practice (GCP) (1), 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 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

22.3 Trademarks and Copyright

23 BIBLIOGRAPHY

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8. *Busch S, Giere T, Lenarz T, Maier H. Comparison of audiologic results and patient satisfaction for two osseointegrated bone conduction devices: results of a prospective study. Otol Neurotol. 2015;36(5):842–848.*

9. Dmitrienko A, D'Agostini R.B. " Multiplicity Considerations in Clinical Trials", N ENGL J MED 378 and 2018, 22 may.

10. *MEDDEV 2.7/3, revision 3, May 2015, CLINICAL INVESTIGATIONS: SERIOUS ADVERSE EVENT REPORTING UNDER DIRECTIVES 90/385/EEC AND 93/42/EEC.*

11. *(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-involvin.*

CHANGE HISTORY

Version	Change	Rationale
1.0	Original version	
2.0	Section 2, 7.1, 7.2.2 and 8.5. Added section 17.1	Changes due to questions from Swedish MPA
3.0	Section 2, 8.4, 8.5, 11.4.2,	Updates due to conditional approval by the Swedish MPA
4.0	Section 8.4	Updated due to reuse of IMD.