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PROTOCOL

Clinical Evaluation of the Cochlear Nucleus® CI532 Cochlear Implant in Adults

Investigation Number: CLTD5685

Clinical Study

Version 7.0

June 28, 2019

Study Sponsor:

Cochlear Limited
1 University Avenue
Macquarie University, NSW 2109
Australia

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Investigator Responsibilities

I, the undersigned, am responsible for the conduct of the study at the site below and by my signature below, I confirm that I have read, understand and will strictly adhere to the study protocol, "**Clinical Evaluation of the Cochlear Nucleus® CI532 Cochlear Implant in Adults**"

Clinical Investigational Site

Principal Investigator's Name (print)

Title

Signature

Sponsor Representative

Title

Signature

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Clinical Investigational Synopsis

Title	Clinical Evaluation of the Cochlear Nucleus® CI532 Implant in Adults
Study Sites	Up to 15 sites
Study Duration per subject	Up to 15 Months (12 months post sound processor activation)
Study Population	Up to 100 adult CI532 candidates
Design Overview	The clinical investigation will be conducted as a nonrandomized, single-subject, repeated-measures design in which each subject serves as his/her own control. Study participants will be evaluated during 7 scheduled visits, using both objective and patient reported outcome measures.
Primary Objective	To evaluate pre and post implantation speech recognition in quiet in the implanted ear alone.
Secondary Objectives	1. To evaluate pre and post implantation speech recognition in noise in the implanted ear alone 2. To evaluate pre and post implantation Health Utility
Study Intervals	Preoperative, Surgery, Initial Activation, 1, 3, 6 and 12 months post-activation
Primary Endpoint	Improved group mean CNC word recognition in quiet measured at 6 months post sound processor activation compared to the group mean score in the preoperative, best unilateral condition

Secondary Endpoint	1. Improved group mean AzBio sentence in noise score (SNR +10 dB) measured at 6 months post sound processor activation compared to the group mean score in the preoperative, best unilateral condition 2. Group mean Health Utility Index score (HUI) at 6 months post sound processor activation will be superior to the score measured preoperatively.

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Glossary

Term	Definition
AE	Adverse Event
CRF	Case Report Form
CI500	CI500 series implants (CI512, CI522, CI532)
CP1000	NEO-XS System Sound Processor
CR310	NEO-XS System Project Remote Control
iPhone	Apple mobile smartphone
MEA	Monitor Earphone Adaptor
MFi	Made For iPhone
NEO-XS	A new processor chip building on the NEO-Ana and NEO-Dig chips used in Nucleus 6 NEO-XS combines analog and digital circuitry into a single package to achieve reductions in size and power requirements.
SAE	Serious Adverse Event
Best Unilateral Condition	Best postoperative unilateral listening condition referring to either Electric-Only or Hybrid Stimulation (defined below).
Electric-Only Stimulation	Electric-Only hearing delivered via the cochlear implant alone. During testing, the cochlear implant will be used in Electric-Only mode and the contralateral ear should be plugged.  **CI**

Term	Definition
Hybrid Stimulation	Combination of acoustic and electric hearing, in the same (implanted) ear. During testing, the cochlear implant will be used in Hybrid mode and the contralateral ear should be plugged.  **CI + HA**
Best Bilateral Listening Condition	Best postoperative bilateral listening condition referring to either Bimodal or Combined Stimulation (defined below).
Bimodal Stimulation	Electric-Only hearing via the cochlear implant in the implanted ear, in addition to acoustic hearing through a hearing aid in the contralateral ear. During testing, the cochlear implant will be used in the Electric-Only mode and tested in combination with the hearing aid on the contralateral ear. **HA**  **CI**
Combined Stimulation	Use of acoustic hearing bilaterally, with amplification, in addition to electric hearing via the cochlear implant. During testing, the cochlear implant will be used in Hybrid mode and tested in combination with the hearing aid on the contralateral ear. **HA**  **CI +**

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1.0 Introduction

Placement of an electrode array influences several parameters including scalar location, insertion depth, and perimodiolar position, each of which can affect speech recognition in patients (Skinner et al., 2007; Aschendorff et al., 2007; Finley et al., 2008; Holden et al 2013).

Pre-curved arrays such as the Contour Advance™ (CA) up until now have required a somewhat flexible metallic "stylet" to hold the electrode straight at the point of first introduction into the cochlea to avoid premature curling of the electrode array. It is recommended that the electrode array is to be advanced off the stylet™ (AOS) such that it follows the trajectory of the basal turn of the cochlea due to its curved shape. In this way contact with the lateral wall, which may produce trauma, may be avoided unlike for a "straight" array. Necessarily the cross-sectional area of the CA is somewhat larger than may be required for a non-stylet "straight" array and there is always some chance that the stiffer array-stylet combination could still produce trauma if deployment of the electrode is not well handled. Either a classic insertion technique or a poorly-handled AOS technique may result in the electrode array dislocating between scala tympani and scala-media or scala-vestibuli, thus producing trauma to the interstitial membranes. In addition an electrode array in scala vestibuli is at a greater distance from the stimulation target (spiral ganglion cells) compared to one in scala tympani – thus current paths to these cells may be irregular and stimulation will be less selective, potentially reducing performance (Holden et al., 2013).

The new CI532 cochlear implant has a pre-curved, perimodiolar electrode array, which does not incorporate a lumen and stylet; instead it has a thin electrode carrier which is introduced into the cochlea through a straightening sheath (Fig 1). The cross-sectional area of the electrode array is approximately 40% of that of the CA and thus it is overall less stiff than the CA; these two factors may allow the electrode array to take up a position within scala tympani closer to the modiolus. Insertion of the array will be achieved using the advance-through-the-sheath technique this ensures that intra-cochlear trauma is minimized and offers the potential for hearing preservation in as many cases as possible.

Imaging and 3D reconstruction of pre- and post-operative CT scans has been used at Washington University School of Medicine (WUSM) to determine the position of implanted electrodes within the cochlea (Skinner et al., 2007; Teymouri et al., 2011; Holden et al., 2013). Scalar location (i.e., scala tympani, ST vs scala vestibuli, SV), insertion depth and wrapping factor can all be determined through this process.

Given the design characteristics of the CI532, it is postulated that the CI532 electrode will be placed more consistently in the scala tympani, perimodiolar

position will be less variable and trauma to the cochlea structure will be minimized resulting in less variable outcomes across individual subjects once important subject characteristics are considered (such duration of hearing loss).

Subjects in this study will be fit with the CP1000 Sound Processor. The CP1000 Sound Processor is the smallest and lightest BTE processor designed by Cochlear, Ltd. The CP1000 was designed to function in a similar manner to the predicate Nucleus 6 BTE CP900 Series Sound Processors but with new architecture, industrial design and resulting cosmetic and connectivity improvements. As part of this, function and user satisfaction of the CP1000 Sound Processor in newly implanted adults will be evaluated.

2.0 Study Design Overview

The clinical investigation will be conducted as a multicenter, prospective, nonrandomized, single-subject, repeated-measures design in which each subject serves as his/her own control. This approach accommodates the heterogeneity that characterizes hearing-impaired populations. Blinding procedures are not appropriate for this trial design, as it is not possible to conceal the presence, or absence, of a cochlear implant (CI) system from recipients and/or clinical Investigators.

Study participants will be evaluated during six scheduled visits, using both objective measures and patient reported outcomes. Speech perception measures will be used to evaluate speech understanding in quiet and noise. Of primary interest is speech understanding in the implanted ear but speech understanding will also be evaluated in the bilateral listening condition. Questionnaire data will also be collected that will document subjective hearing performance, connectivity, streaming, phone use, comfort, retention, ease of use, and controls associated with the CP1000 Sound Processor(s) during take-home use. Additional patient reported outcomes will capture subject's perceived quality of life and also evaluate cognitive skills

2.1 Study Length

The expected duration of each subject's participation in the clinical investigation is 15 months.

3.0 Device Description

3.1 CI532 Cochlear Implant

The commercially available Nucleus® CI532 cochlear implant will be used in this study. The CI532 consists of a CI500 Series receiver/stimulator and a pre-curved, modiolar electrode array (EA32).

Figure 1. Left: The EA32 electrode array loaded in the sheath (upper), advanced through the sheath, and with the sheath removed as in final situation (lower). Right: Nucleus CI532 cochlear implant.

3.2 CP1000 Sound Processor

The CP1000 Sound Processor hardware consists of a single push button control, a replaceable top microphone cover that contains a pair of permanently mounted covers, and an integrated coil and coil cable. There is no accessory port on the CP1000 Sound Processor, but it is compatible with Cochlear's existing range of wireless accessories. A new Monitor Earphone Adaptor (MEA) and the Phonak Roger Receiver module are both compatible for use with Monitor Earphones and compatible Roger Phonak transmitters. The CP1000 Sound Processor also incorporates a telecoil.

The CP1000 Sound Processor is compatible with:

- A wireless programming adaptor for wireless programming sessions.
- Hybrid receivers in three new receiver sizes.

- Cochlear's range of Wireless Accessories (Cochlear Phone clip, Cochlear Mini Microphone, Mini Microphone 2 and 2+, and Cochlear TV Streamer).
    - These accessories are also compatible with the CP910 and CP920 Sound Processors and certain GN ReSound Hearing Aids, meaning that bimodal streaming is available.

In addition, the CP1000 Sound Processor can be linked to GN Resound hearing aids via the fitting software to enable bimodal pairing to Apple devices providing access to bimodal control and direct audio streaming.

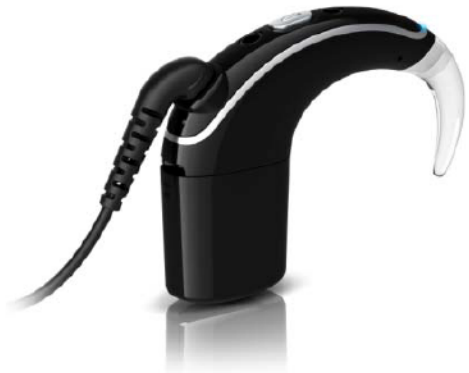

Figure 2: Image of the CP1000 Sound Processor in cochlear implant configuration

The CP1000 Sound Processor is controlled by the following:

- Recipient App on the iPhone/iPod Touch.
- iOS Accessibility options
- CR310 Remote Control.
- Sound Processor button

With the Aqua+ coil and cable, and rechargeable batteries, the CP1000 Sound Processor will be waterproof up to IP68[1].

Various retention accessories are compatible with the CP1000 Sound Processor, including:

[1] No Hybrid in this configuration.

- Earhooks in small, medium, and large sizes, and the Tamper Resistant Earhook.
- Snugfit and Hugfit to hold the sound processor more securely in place.
- Custom Earmold Adaptor for custom earmolds to be attached to the sound processor.
- Shoulder worn adaptor to clip sound processor on to clothing and off the head.

3.3 Programming Software Description

3.3.1 Custom Sound 5

Custom Sound 5 will include support for fitting the CP1000 Sound Processor with compatible implants and for this study specifically the CI532 implant.

The Custom Sound Data Viewer will show CP1000 Sound Processor logs (equivalent to CP900, plus amount of time spent streaming directly from the phone and Roger Receiver).

Custom Sound 5 will also include updates to Hybrid fitting, in particular:

- Receiver and vent sizes incorporated in prescription targets
- Ability to enter both bone conduction and air conduction audiometric thresholds

Custom Sound 5 will implement a new mechanism that exchanges Hearing Instrument identification between a CP1000 Sound Processor and compatible GN ReSound Hearing Aid. This mechanism is in place to support MFi pairing to Apple devices.

4.0 Subject Population

Study sites will enroll up to 100 adult cochlear implant candidates at up to 15 North American cochlear implant centers.

Subjects must meet the following inclusion and exclusion criteria:

4.1 Inclusion Criteria

1. Adults 18 years or older who have a bilateral postlinguistic sensorineural hearing loss.
2. Limited benefit from amplification as defined by test scores of 40% correct or less in the ear to be implanted and 50% or less in the contralateral ear on a recorded monosyllabic word test

I. Consistent with the Minimum Speech Test Battery (2011), it is required that all subjects be evaluated at 60 dBA presentation level.

3. Bilateral moderate sloping to profound hearing loss
4. Minimum of 30 days experience with appropriately fit bilateral amplification, fit using the standardized NAL fitting method
5. Proficient in English
6. Ability to complete testing

4.2 Exclusion Criteria

1. Previous cochlear implantation
2. Pre-linguistically deafened (onset of hearing loss at less than two years of age)
3. Ossification or any other cochlear anomaly that might prevent complete insertion of the electrode array
4. Duration of severe to profound hearing loss greater than 20 years
5. Diagnosis of retro-cochlear pathology
6. Diagnosis of auditory neuropathy
7. Unrealistic expectations on the part of the subject regarding the possible benefits, risks, and limitations that are inherent to the surgical procedure and use of the prosthetic device
8. Unwillingness or inability to comply with all investigational requirements
9. Additional cognitive, medical or social handicaps that would prevent completion of all study requirements

5.0 Study Objective and Endpoints

5.1 Objectives

Primary Objective

To evaluate pre and post implantation speech recognition in quiet scores in the implanted ear alone.

Secondary Objectives

1. To evaluate pre and post implantation speech recognition in noise scores in the implanted ear alone
2. To evaluate pre and post implantation Health Utility

5.2 Study Endpoints

Primary Endpoint

Improved group mean CNC word recognition in quiet measured at 6 months post sound processor activation in the best unilateral condition[2] compared to the group mean score obtained in the preoperative, unilateral aided –ear to be implanted condition.

Secondary Endpoints

1. Improved group mean AzBio sentence in noise score (SNR +10) measured at 6 months post sound processor activation in the best unilateral condition compared to the group mean score in the preoperative, unilateral aided – ear to be implanted condition
2. Improved group mean HUI3 score measured at 6 months post sound processor activation compared to the scores measured preoperatively

5.3 Hypotheses

5.3.1 Primary Hypothesis

H_0: Group mean CNC word scores in the best unilateral listening condition measured at 6 months post sound processor activation will not be superior to the group mean score in the preoperative, unilateral condition.

H_0: $\mu_{Post} - \mu_{Pre} \leq 0$

[2] This may be hybrid hearing in subjects with aidable low frequency hearing or electric alone for those who do not have aidable low frequency hearing

H_1: Group mean CNC word scores in the best unilateral listening condition measured at 6 months post sound processor activation will be superior to the group mean score in the preoperative, unilateral condition.

$$H_1: ì_{Post} - ì_{Pre} > 0$$

Where $ì_{Pre}$ is the CNC word score in quiet obtained with a hearing aid preoperatively in the ear to be implanted, and $ì_{Post}$ is the CNC word score in quiet obtained at 6 months post sound processor activation in the treated ear. Unilateral testing will be undertaken using the same test ear, pre vs post implantation.

5.3.1 Secondary Hypotheses

Secondary Hypothesis 1

H_0: Group mean AzBio sentence in noise scores (SNR +10) in the best unilateral listening condition measured at 6 months post sound processor activation will not be superior to the group mean score in the preoperative, unilateral condition.

$$H_0: ì_{Post} - ì_{Pre} \leq 0$$

H_1: Group mean AzBio sentence in noise scores (SNR +10) in the best unilateral listening condition measured at 6 months post sound processor activation will be superior to the group mean score in the preoperative, unilateral condition.

$$H_1: ì_{Post} - ì_{Pre} > 0$$

Where $ì_{Pre}$ is the AzBio Sentence score in noise obtained with a hearing aid preoperatively in the ear to be implanted, and $ì_{Post}$ is the AzBio Sentence score in noise obtained at 6 months post sound processor activation in the treated ear. Unilateral testing will be undertaken using the same test ear, pre vs post implantation.

Secondary Hypothesis 2

H_0: Group mean overall utility score (HUI3) at 6 months post sound processor activation will not be superior to the scores measured preoperatively.

$$H_0: ì_{Post} - ì_{Pre} \leq 0$$

H_1: Group mean overall utility score (HUI3) at 6 months post sound processor activation will be superior to the scores measured preoperatively.

$$H_1: ì_{Post} - ì_{Pre} > 0$$

Where $ì_{Pre}$ is the score obtained preoperatively, and $ì_{Post}$ is the score obtained at 6 months post sound processor activation.

5.4 Additional Analyses

- Observation of the audiometric threshold at 500 Hz at each interval (IA, 1, 3, 6 and 12 months) with subjects stratified into 2 groups based on their age at time of enrolment:
    - < 70 years
    - ≥ 70 years
- Evaluation of the effect of age on speech perception in quiet and noise in both the unilateral and bilateral conditions, with subjects stratified into 2 groups based on their age at time of enrolment:
    - < 70 years
    - ≥ 70 years
- Evaluation of pre and post implantation patient reported outcomes:
    - Mini Tinnitus Questionnaire (miniTQ)
    - Patient Based Resource and Expenditure Questionnaire
    - Speech, Spatial, Qualities of Hearing Scale (SSQ)
    - The Montreal Cognitive Assessment (MoCA)
- Evaluation of user satisfaction with the CP1000 Sound Processor and related components
- Measurement of the CI532 electrode array scalar location and modiolar proximity through reconstructed CT images
- Evaluation of word recognition in quiet and noise at 6 months in the bilateral listening condition – for some subjects this will be the bimodal condition (CI + contralateral hearing aid), and for others this will be the combined condition CI + Acoustic hearing (same ear) + contralateral hearing aid). Additionally a subgroup analysis will be done for: Subjects using bimodal hearing and subjects using combined hearing. Differences between and within the subgroup will be evaluated.
- Subgroup analysis will be done for: Subjects using hybrid hearing (acoustic + electric in the implanted and subjects using electric alone. Differences between and within the subgroup will be evaluated for primary and secondary endpoints.

No formal hypotheses will be generated for these additional analyses. The intention is to provide clinical guidance and experience on the use of the CI532 cochlear implant as well as the fitting and use associated with the CP1000 Sound Processor on a group of newly implanted cochlear implant recipients.

6.0 Investigational Procedures

6.1 Subject Identification

To maintain confidentiality, subject names will not be recorded on any study document other than the informed consent form. All individuals who provide informed consent (sign the informed consent form) are considered enrolled into the study and will be assigned a unique identifier. A unique alphanumeric code will identify each subject throughout the course of the study. For example, US01-532-0000, where:

- US = United States,
- 01 = a sequential numeral corresponding the order in which a subject is enrolled into the study for a given study site, in this case this would correspond to the first subject recruited into the study for a particular site,
- 532 = an abbreviation for the study, in this case 532 for the CI532 cochlear implant,
- 0000 = a unique, numeric study site identification.

6.2 Release of Medical Information

Subjects must sign a release that authorizes access of medical records to the study Sponsor, Investigators, monitors, and the Food and Drug Administration (FDA), prior to proceeding with any screening evaluations.

6.3 Description of Study Measures

6.3.1 Clinical Audiological Testing

6.3.1.1 Pure-tone Audiometry

Unaided audiometric thresholds will be obtained for each ear, with insert earphones, using the standard audiometric technique for pure-tone air-conduction testing (refer to Appendix A for required specifications and calibration requirements). Aided audiometric thresholds will be obtained for each ear in the sound field using warble tones and the standard audiometric technique with the speakers positioned at 0 degrees azimuth relative to the subject's head.

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Note: As these subjects may have measureable low-frequency hearing, it is important that appropriate consideration be made for masking (procedure outlined in Appendix B) or plugging the contralateral ear during unilateral testing in the sound field. Testing, for both ears, will include the following:

Frequency-specific thresholds at standard audiometric frequencies for both ears.

- Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
- Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz

An aided audiogram will be performed for both ears at the following frequencies using warble tones:

- Aided thresholds: 125, 250, 500, 750, 1000, 2000, 3000, 4000 Hz

6.3.1.2 Consonant-Nucleus-Consonant (CNC) Word Recognition Test

The CNC Word Test (Peterson & Lehiste, 1962) consists of 10 recorded lists of 50 monosyllabic words. For this study, two lists will be administered per test condition and scored as the number of words correct, which will be expressed as a percentage of the total number of items presented.

6.3.1.3 AzBio Sentences

The AzBio Sentence Test (Spahr & Dorman, 2005) is a validated test that consists of 15 lists of 20 sentences each. Each list includes 5 sentences from each of 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. Subjects will be tested using a configuration of speech at 0º azimuth in quiet. Subjects will be tested using a configuration of speech and noise at 0º azimuth at +5 dB and +10 dB SNR.

6.3.2 Patient Reported Outcome Measures

6.3.2.1 Mini Tinnitus Questionnaire

The Mini Tinnitus Questionnaire (Mini-TQ) is an abbreviated version of the Tinnitus Questionnaire (TQ) (Hiller & Goebel, 2006). The 12-item Mini-TQ defines a general dimension of distress that has a high degree of correlation ($r > 0.90$) with the full TQ. This questionnaire will be completed by subjects preoperatively, and the follow up measure will be completed at six months post activation.

6.3.2.2 Health Utility Index Mark 3 (HUI3)

The HUI3 (Furlong, Feeny, Torrance,& Barr, 2001) is a validated, 15-item population-based health utility instrument that postulates the domains of health as

hearing, vision, speech, emotion, pain, ambulation, dexterity, cognition, and self-care. Respondents are mapped into 1 of 972,000 unique health states depending on their functional capacity.

6.3.2.3 Patient Based Resource and Expenditure Questionnaire

This questionnaire developed by Cochlear focuses on costs associated with hearing loss both pre-operatively and following cochlear implantation

6.3.2.4 Speech, Spatial, Qualities (SSQ)

The SSQ (Gatehouse & Noble, 2004) will be used as a subject self-assessment in three categories (speech hearing rating scale, spatial rating scale, and sound qualities rating scale).

6.3.2.5 The Montreal Cognitive Assessment (MoCA)

The MoCA (Nasreddine et al., 2005) was designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The MoCA has been validated for 55-85 year olds.

6.3.2.6 Sound Processor Questionnaire

The listening experience sound processor questionnaire is an in-house developed questionnaire designed to collect subjective ratings on each subject's experiences with their current hearing technology. This questionnaire is designed to be administered at different time points and will provide an opportunity to evaluate changes to ratings after use with new technology.

6.3.2.7 Hearing History Questionnaire

The Hearing History Questionnaire is a questionnaire that will be completed preoperatively. Subjects will be asked about to their experiences with their hearing prior to implantation. Some of these responses will be paired with the responses on the Sound Processor Questionnaire for analysis.

6.3.2.8 Imaging

Preoperative CT scans are optional and will be undertaken at the discretion of the investigator. An intraoperative X-ray will be obtained following the placement of the electrode and prior to closing. Following surgery subjects will undergo a CT scan according to the specifications provided by the study sponsor. Postoperative analysis of the CT scan will be done via reconstruction to determine electrode position and distance to the modiolus.

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6.4 Procedures

6.4.1 Pre-operative Procedure

6.4.1.1 Preoperative Candidacy Evaluation

6.4.1.1.1 Informed Consent

A preoperative interview (as part of the informed consent process) will be conducted by the surgeon and/or audiologist to inform the candidate about all aspects of implantation with a cochlear implant, study expectations, surgical procedure, as well as the evaluation schedule. The risks of surgery shall be explained to the subject as outlined in the Informed Consent Form. These include the risks associated with general anesthesia, as well as other risks such as loss of residual hearing, facial paralysis, dizziness, meningitis, postoperative discomfort, and flap complications. The potential limitations and advantages of cochlear implantation shall also be explained.

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 candidate will be offered the opportunity to take the form home to discuss with family members should they choose to do so. If they sign the Informed Consent Form, the candidate will then be given a copy of the signed Informed Consent Form to take home.

A candidate is not considered enrolled until a properly executed Informed Consent Form has been obtained along with the results of the preoperative candidacy evaluation.

6.4.1.1.2 Candidacy Baseline Assessment

- Frequency-specific thresholds at standard audiometric frequencies for each ear
    - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
    - Bone conduction: 250, 500, 750, 1000, 2000, 3000, 4000 Hz

Note: Clinician will need to confirm the subject's response to any pure tone stimulus presented at 125 and 250 Hz as auditory "heard" versus vibrotactile "felt" and record the response accordingly.

- An aided audiogram will be performed at the following frequencies using warble tones:
    - Aided thresholds: 125, 250, 500, 750, 1000, 2000, 3000, 4000 Hz

        - Unilateral each ear with contralateral ear plugged
    - Aided speech recognition in quiet:
        - CNC Words: Two lists at 60 dB(A) in each of the following conditions
            - Unilateral aided each ear with contralateral ear plugged
            - Bilaterally aided
    - Aided speech recognition in noise:
        - AzBio sentences: One list at 65 dBA with a +10 dB signal to noise speech and noise presented at 0 degrees azimuth
            - Unilateral aided each ear with contralateral ear plugged
            - Bilaterally
        - AzBio sentences: One list at 65 dBA with a +5 dB signal to noise speech and noise presented at 0 degrees azimuth
            - Unilateral aided each ear with contralateral ear plugged
            - Bilaterally

NOTE: The contralateral ear will be plugged/muffed for all audiological testing in the unilateral listening condition

- Patient Reported Outcomes:
    - Hearing History Questionnaire
    - Mini-TQ
    - SSQ
    - HUI3
    - Patient Based Resource and Expenditure Questionnaire (PBRE)
    - MoCA (subjects 55 – 85 years old)

All subjects will be tested with appropriately fit amplification. The hearing aids will be fit according to standard clinical practice of meeting prescribed target gain- refer to Appendix B for a suggested hearing aid fitting guideline.

For consistency and to reduce variability, subjects who meet the inclusion and exclusion criteria and elect to enrol into the study will be fit with a compatible GN ReSound hearing aid on the contralateral ear and will be required to use the hearing aid to the primary study endpoint of 6 months.

Any adverse events or device deficiencies will be reported.

6.4.1.1.3 Surgical Procedure

The surgical approach will be cochlear implantation via posterior tympanotomy as described in the CI532 Physician's Guide. Insertion of the array will be achieved using the advance-through-the-sheath technique described in the Physician's guide.

The surgeon is required to complete following each surgery:

- A surgical questionnaire
- X-ray: Consistent with the Nucleus® CI532 cochlear implant with Slim Modiolar electrode Physician's Guide on page 81, an X-ray will be obtained prior to closure (preferably a lateral or modified Stenvers view) to confirm proper electrode placement.
- Neural Response Telemetry: Optional

6.4.1.1.4 Initial Activation

At the initial activation appointment, the following procedures will be completed:

- Frequency-specific thresholds at standard audiometric frequencies for each ear:
  - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
  - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz
- The initial activation will be performed according to standard clinical procedures using Custom Sound and the recommended default programming settings for the CP1000 Sound Processor
- In the event that a subject retains aidable hearing in the implanted ear, they will also be fitted with the acoustic component. The acoustic component will be appropriately fit using the National Acoustics Laboratories' hearing aid fitting strategy (as used preoperatively for hearing aid verification and outlined in Appendix B) to assess the degree to which real-ear targets are met for each subject. Fitting methodology with the CP1000 Sound Processor acoustic component is no different than that of conventional acoustic hearing aids.
- An anonymized .cdx file will be provided to the study sponsor.
- CT Scan (prior to the 3 month visit)

6.4.1.1.5 One Month Post activation

At 1 month post activation, the following procedures will be completed:

- Mapping review will be performed according to standard clinical procedures using Custom Sound and the default programming settings for the CP1000 Sound Processor.
- Frequency-specific thresholds at standard audiometric frequencies for each ear:
    - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
    - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz
- If necessary mapping will be performed according to standard clinical procedures using Custom Sound and the recommended default programming settings for the CP1000 Sound Processor.
- An anonymized .cdx file will be provided to the study sponsor
- Post-operative CT Scan if not yet completed.

6.4.1.1.6 Three Month Post activation

At 3 months post activation, the following procedures will be completed:

- Mapping review will be performed according to standard clinical procedures using Custom Sound and the default programming settings for the CP1000 Sound Processor.
- Frequency-specific thresholds at standard audiometric frequencies for both ears.
    - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
    - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz

Note: In any case where a total hearing loss is documented in the implanted ear at two consecutive postoperative test intervals, pure tone audiometric testing for that ear may be omitted for subsequent evaluations

Subjects with post-operative aidable low frequency hearing; best unilateral refers to Hybrid Hearing (Acoustic + Electric in the implanted ear). These subjects will be tested in 2 unilateral conditions:

1. Best unilateral - Hybrid Hearing and
2. Electric Alone

Subjects who do not have aidable low frequency hearing best unilateral refers to Electric only, these subjects will be tested only one condition.

- Speech recognition in **quiet**:
    - CNC Words: presented at 60 dB A
        - Best unilateral condition, implanted ear with contralateral ear plugged
        - Electric alone condition, implanted and contralateral ear plugged (if applicable)
- Speech recognition in **noise:**
    - AzBio sentences presented at 65 dBA with a +10 dB signal to noise ratio speech and noise at 0 degrees azimuth
        - Best unilateral condition, implanted ear with contralateral ear plugged
        - Electric alone condition, implanted and contralateral ear plugged (if applicable)
- An anonymized .cdx file will be provided to the study sponsor

6.4.1.1.7 Six Months Post activation

At 6 months post activation, the following procedures will be completed:

- Frequency-specific thresholds at standard audiometric frequencies for both ears.
    - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
    - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz

Subjects with post-operative aidable low frequency hearing; best unilateral refers to Hybrid Hearing (Acoustic + Electric in the implanted ear). These subjects will be tested in 2 unilateral conditions:

1. Best unilateral - Hybrid Hearing and
2. Electric Alone

Subjects who do not have aidable low frequency hearing best unilateral refers to Electric only, these subjects will be tested only one condition.

- Speech recognition in **quiet**:
  - CNC Words: presented at 60 dB A
    - Best unilateral condition, implanted ear with contralateral ear plugged
    - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
    - Bilateral listening condition[3]
- Speech recognition in **noise**:
  - AzBio sentences: One list at 65 dBA with a +10 dB signal to noise ratio speech and noise at 0 degrees azimuth
    - Best unilateral condition, implanted ear with contralateral ear plugged
    - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
    - Bilateral listening condition[4]
  - AzBio sentences: One list at 65 dBA with a +5 dB signal to noise ratio speech and noise at 0 degrees azimuth
    - Best unilateral condition, implanted ear with contralateral ear plugged
    - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
    - Bilateral listening condition[4]
- Mapping will be performed according to standard clinical procedures using Custom Sound and the default programming settings for the CP1000 Sound Processor.
- An anonymized .cdx file will be provided to the study sponsor
- Patient Reported Outcomes:
  - Sound Processor Questionnaire

[3] Refers to subjects preferred everyday bilateral listening mode: May be CI + Acoustic (Contralateral ear) or CI + Acoustic (same ear)-(Hybrid Hearing) + Acoustic contralateral ear

- SSQ
- Mini TQ
- HUI3
- Patient Based Resource and Expenditure Questionnaire (PBRE)
- MoCA

6.4.1.1.8 12 Months Post Activation

At 12 months post activation, the following procedures will be completed:

- Frequency-specific thresholds at standard audiometric frequencies for each ear.
  - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
  - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz

Subjects with post-operative aidable low frequency hearing; best unilateral refers to Hybrid Hearing (Acoustic + Electric in the implanted ear). These subjects will be tested in 2 unilateral conditions:

1. Best unilateral - Hybrid Hearing and
2. Electric Alone

Subjects who do not have aidable low frequency hearing best unilateral refers to Electric only, these subjects will be tested only one condition.

- Speech recognition in **quiet**:
  - CNC Words: Two lists at 60 dB A
    - Best unilateral condition, implanted ear with contralateral ear plugged
    - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
- Speech recognition in **noise**:
  - AzBio sentences: One list at 65 dBA with a +10 dB signal to noise ratio speech and noise at 0 degrees azimuth
    - Best unilateral condition, implanted ear with contralateral ear plugged

        - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
        - Best Bilateral listening condition[4]
    - AzBio sentences: One list at 65 dBA with a +5 dB signal to noise ratio speech and noise at 0 degrees azimuth
        - Best unilateral condition, implanted ear with contralateral ear plugged
        - Electric alone condition, implanted and contralateral ear plugged (if appropriate)
        - Best Bilateral listening condition[5]
- Mapping will be performed according to standard clinical procedures using Custom Sound and the default programming settings for the CP1000 Sound Processor.
- An anonymized .cdx file will be provided to the study sponsor
- Patient Reported Outcomes:
    - Mini TQ

Additional activities:

Subjects may return to the clinic for unscheduled sessions to review, update and/or load Sound Processor settings. Non-study follow-up visits may also take place at the discretion of the study site as part of routine care.

If study subjects are clinically suitable for bimodal stimulation (i.e., a cochlear implant on one ear and a hearing aid on the contralateral ear) and are fit bimodally at initial activation, subjects will be encouraged to continue to use this configuration through 6-months post activation.

6.5 Summary of Data Collection Visits

Each subject will participate in 7 scheduled evaluation sessions. Subjects will be seen preoperatively, at surgery, at the initial activation and at 1, 3, 6 and 12 months

[4] Refers to subjects preferred everyday best bilateral listening mode: May be Bimodal (CI + Acoustic (Contralateral ear)) or Combined - CI + Acoustic (same ear)-(Hybrid Hearing) + Acoustic in contralateral ear

post activation. Visit windows are unrestricted, however for the 1, 3, 6 and 12 month visits, deviations from these intervals by more than +/- 4 weeks will be reported on in the clinical investigation report.

Additional, unscheduled sessions may be required to review, update and load Sound Processor settings (including software, MAPs and input processing).

Table 1: Data Collection Visit Schedule.

Measure	Pre-Op	Surgery	Initial Activation	1 mth	3 mth	6 mth	12 mth
Informed Consent	X						
Hearing History	X						
Audiometric (AC & BC)	X		X	X	X	X	X
CNC Words	X				X	X	X
AzBio N	X				X	X	X
SP Qnaire						X	
Mini TQ	X					X	X
SSQ	X					X	
HUI	X					X	
PBRE	X					X	
MoCA	X					X	
Imaging	X	X	X				
AEs and DDs		X	X	X	X	X	X

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7.0 Reporting Process for Adverse Events and Device Deficiencies

7.1 Definitions

7.1.1 Adverse Event (AE)

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 investigational medical device.

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

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

NOTE 3 For users or other persons, this definition is restricted to events related to investigational medical devices.

7.1.2 Adverse device effect (ADE)

An adverse device effect is an adverse event related to the use of an investigational medical device.

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

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

7.1.3 Device deficiency (DD)

A device deficiency 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.

7.1.4 Serious Adverse Event (SAE)

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

- led to death
- led to serious deterioration in the health of the subject, that either resulted in

1) a life-threatening illness or injury, or
2) a permanent impairment of a body structure or a body function, or
3) in-patient or prolonged hospitalization, or
4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

- led to fetal distress, fetal death or a congenital 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 serious adverse event.

7.1.5 Serious adverse device effect (SADE)

A serious adverse device effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

7.1.6 Unanticipated Adverse Device Effects

Unanticipated adverse device effects refer to any event that represents a "serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects." [FDA 21 CFR 812.3(s)]

7.2 Assessment and Reporting of Adverse Events and device deficiencies

To monitor subject safety throughout this IDE study, adverse events and device deficiencies will be recorded. Information on all adverse events will be maintained by event type. The investigator will complete an Adverse Event and/or Device Deficiency form if any adverse event or device deficiency is reported or observed for a subject during this IDE, even if the event was acknowledged as a risk factor in the Informed Consent form.

Investigators are to inform their respective Institutional Review Boards (IRBs) and Cochlear Americas immediately if an unanticipated adverse device effect is suspected (no more than 10 working days after the investigator learns of the effect). If the case is determined to be an unanticipated adverse device effect, the investigator will fill out an "Unanticipated Adverse Device Effect Form." Cochlear

Americas will report the results of an evaluation of the unanticipated adverse device effect to the FDA and all other reviewing IRBs and investigators within 10 working days after first receiving notice of the event.

The investigator shall report all serious adverse events and device deficiencies that could have led to a serious adverse event to the sponsor without delay.

The Sponsor will report all adverse events to the FDA and respective IRBs through the required annual or biannual progress reporting process.

The details of the Medical Monitor responsible for the clinical investigation are:

Name of contact person of the sponsor	[redacted]
Phone number (business hours)	[redacted]
Phone number (after hours)	[redacted]
E-mail	[redacted]

7.3 Protocol Deviations

The investigator is not allowed to deviate from the protocol except under emergency circumstances to protect the rights, safety and well-being of the subjects. Such deviation shall be documented and reported to the Sponsor and the IRB as soon as possible.

The procedure for recording and reporting protocol deviations shall be via a Protocol Deviation form. Analysis of protocol deviations shall be undertaken by the Sponsor and reported to the FDA and IRBs as required.

8.0 Study Completion

8.1 Completed Subjects

Once the 12 month post-activation visit is completed, the subject will be deemed complete. Subjects will receive a sound processor for their daily use after the study is complete (the CP1000 if it is approved by that time or any other approved sound processor) and will continue to receive standard clinical follow-up care at their cochlear implant facility after the study.

8.2 Discontinued Subjects

Any subject may voluntarily discontinue the study at any time without prejudice. The Investigator may discontinue a subject from the study at any time if (s)he considers

that remaining in the study compromises the subject's health or the subject is not sufficiently cooperative. In either event, the reason(s) for discontinuation should be recorded on a study withdrawal form, provided as part of the case report form packet for the study. Possible reasons for study discontinuation include the following:

- AE necessitating discontinuation from the study
- The subject is lost to follow-up
- Voluntary decision to withdraw consent made by the subject
- Investigator decision
- Other reason

In the case of a subject lost-to-follow-up, the Investigator must attempt to contact the subject (or relative/family contact) by phone, email, or letter at least three times. If attempts are unsuccessful, the 'subject withdrawal' form is to be completed in the study file and reported, as appropriate, in required reports to the Sponsor and IRB.

8.3 Premature Study Termination

The Sponsor may terminate the study early in the case of major non-adherence to the protocol, or if it is anticipated that recruitment will not be met for the required number of subjects to complete the study objectives. In the event of premature study termination, the subjects who are already enrolled will be sponsored through study completion.

9.0 Data Analyses

9.1 Study Population

All subjects who are consented into the clinical study will constitute the intention-to-treat (ITT) population for the purposes of adverse event reporting. Only subjects implanted with the CI532 and fit with the CP1000 Sound Processor and completed per the protocol will be considered as the completed cases (CC) population and per protocol (PP).

9.2 Sample Size

The sample size calculation was based on the primary and secondary endpoints.

CNC words

To calculate the minimum sample size required to reject the null hypothesis (H0) that *"Group mean CNC words scores in the best unilateral listening condition*

measured at 6 months post sound processor activation will not be superior to the group mean score in the preoperative, best unilateral condition", the following values were chosen:

- A minimum clinically meaningful difference between pre to post activation at 6 months of 15% for CNC words in quiet, based on clinical consensus.
- An expected standard deviation of difference scores of 22.4% for CNC words in quiet. This SD is based on the estimated standard deviation of difference score data collected in completed clinical studies
- A significance level α = 0.05 (two-tailed).
- A desired power of 0.9 i.e. there is 90% chance of detecting a real change between the experimental programs.

Based on these assumptions for words in quiet, a sample size of 26 subjects is required to achieve a power of 90%.

AzBio

To calculate the minimum sample size required to reject the null hypothesis (H0) that *"Group mean AzBio sentence in noise scores (SNR +10) in the best unilateral listening condition measured at 6 months post sound processor activation will not be superior to the group mean score in the preoperative, best unilateral condition"*, the following values were chosen:

- A minimum clinically meaningful difference between pre to post activation at 6 months of 15% for sentences in noise, based on previous clinical consensus.
- An expected standard deviation of difference scores of 21.3% for AzBio sentences in noise. This SD is based on previous clinical trial data with newly implanted subjects.
- A significance level of α = 0.05 (two-tailed).
- A desired power of 0.9

Based on these assumptions, a sample size of 24 subjects is required to achieve a power of 90%.

HUI

To calculate the minimum sample size required to reject the null hypothesis (H0) that *"Group mean utility score (HUI) at 6 months post sound processor activation*

will not be superior to the scores measured preoperatively.", the following values were chosen:

- A minimum clinically meaningful difference between pre to post activation at 6 months of 0.12 utility score (Grutters et al, 2007)
- An expected standard deviation of difference scores of 0.18, this is a conservative value based on the SD of the difference measured after hearing aid fitting by Grutters et al. (2007)
- A significance level of $\alpha = 0.05$ (two-tailed).
- A desired power of 0.9

Based on these assumptions, a sample size of 26 subjects is required to achieve a power of 90%.

A sample size of up to 100 adult subjects will be enrolled in the clinical investigation, this large sample will allow for additional analyses to be conducted specifically the additional patient reported outcome measures, where a large sample size is typically desired. Additionally the sample size provides greater justification for generalizability to the wider clinical population.

9.3 Control of Type I Error

The hypotheses for the Primary and Secondary Endpoints are to be tested formally according to a fixed sequence testing procedure. This testing procedure is based on the principle of a closed testing procedure and is used to control the type I error. In the fixed sequence testing, all the following superiority tests will be conducted using a two-tailed 95% CI (alpha=0.025 one-sided).

The Primary Endpoint will be tested first. Only if the superiority test for the Primary Endpoint is successful, then the secondary endpoints will be tested. If the superiority test for the Primary Endpoint fails, the testing procedure stops and no further testing will be performed.

9.4 Justification of Pooling Across Study Sites

Pooling data from study sites will be completed based on the following: all sites will have the same protocol, the Sponsor will monitor the sites to assure protocol compliance, and the data gathering mechanism (case report forms and data acquisition) will be the same across all study sites (Meinert, 1986).

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9.5 Missing Data

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.

10.0 Risk Benefit Statement

10.1 Benefits

It is possible but not guaranteed that advances to cochlear implant technology will improve performance or increase usability of devices for future recipients. This investigation will help to inform the future development of potentially new sound processor designs as well as develop the associated clinical guidance when fitting existing cochlear implant patients. There are no direct benefits anticipated for subjects participating in this study.

10.2 Risks

With any cochlear implant mapping, there is a very small risk of unintentional over-stimulation. Subjects may experience sounds during mapping that are uncomfortably loud. Mitigation of this risk is similar to that used during clinical cochlear implant mapping wherein the sound processor is removed from the subjects head and/or the stimulation to the sound processor is ceased in Custom Sound.

11.0 Good Clinical Practices Statement

The study obligations for the Investigator(s) are outlined in guidelines for Good Clinical Practice (GCP), 21 CFR Part 812 (Code of Federal Regulations Part 812 Investigational Device Exemptions), ISO14155:2011 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), and the Declaration of Helsinki.

12.0 Access to Study Documents and Study Monitoring

Investigator(s) will provide access to study documentation including source data for the purposes of monitoring, audits, IRB review, and regulatory inspections.

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13.0 Quality Control and Assurance

Study sites may be subject to Quality audits at any point during the study. Regulatory agencies may conduct inspections during the course of the clinical investigation and after study completion.

14.0 Institutional Review Board

Each site will obtain approval from its designated IRB prior to commencing any study-related activities. A copy of the IRB approval will be kept in the Investigator file(s). Any additional requirements imposed by the IRB and/or regulatory authority shall be followed. The Investigator(s) will submit the appropriate documentation if any necessary extension or renewal of the IRB approval must be obtained.

15.0 Informed Consent Process

Written informed consent shall be obtained from each subject after explaining the rationale for and the details, aims, and objectives of the study, the risks and benefits of the trial treatment (and alternative treatments), and the extent of the patient's involvement. The Investigator is responsible for ensuring that all patients give written informed consent prior to any study-related examination or activity. All patients shall sign and date the Informed Consent Form, and a copy of the Informed Consent Form shall be given to the patient.

The Sponsor and the Investigator(s) shall avoid improper influence on or inducement of the subject, monitor, the Investigator(s) or other parties participating in or contributing to the clinical investigation.

16.0 Confidentiality

A Case Report Form (CRF) will be completed for each study subject, summarizing all clinical and study data. The CRF contains confidential material. Subjects will only be referred to in the CRF by their subject numbers in order to retain subject confidentiality. Specific instructions to complete the CRF shall be provided to the clinical investigation team as appropriate.

The CRFs are to be retained by the Investigator for a period of time as determined by local regulations.

17.0 Protocol Deviations and Amendments

The Investigator must receive prior approval from the Sponsor, and the IRB when necessary, to deviate from the protocol except in cases of emergency to protect the

rights, safety, and well-being of the subjects. Emergency protocol deviations must be documented and reported to the Sponsor and the IRB.

No changes in the protocol or informed consent shall be effected without mutual agreement between the FDA, IRB and the Sponsor. Changes related to the scientific intent of the study shall be documented in the protocol amendment and requires signatures from both the sponsor and the participating investigator.

18.0 Data Management

Data collection is performed using electronic data capture (EDC) on electronic Case Report Forms (eCRFs). Site personnel will be trained on the completion of the eCRFs prior to obtaining their own Login/Password. Access to clinical study information will be based on an individual's role and responsibilities.
In the event that the site requests assistance with data entry from the Sponsor, the Sponsor may assign a non-study related team member to assist the site with data entry.

The application provides hierarchical user permissions for data entry, viewing, and reporting options. All communications between the users and the EDC are encrypted. Web servers are protected by a managed firewall. This application is designed to be in full compliance with International Conference on Harmonization and Good Clinical Practices (ICH-GCP).

19.0 Record Keeping and Retention

All source documents, CRFs, and trial documentation will be kept by the Investigator(s) for the appropriate retention period as stipulated by local regulations and ICH-GCP.

20.0 Device accountability

Investigational devices shall be tracked during the study.

In cases where the investigational devices are commercially released products, the products shall be registered following the standard product registration process.

In cases where a commercially released product is required to facilitate the functionality of the investigational device, the commercial product shall be registered following the standard product registration process.

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21.0 Study Report and Publication

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law.

The aggregate data resulting from this study will be the proprietary information of the Sponsor and may be made public after all data have been analyzed and the study results are available. None of the data resulting from this study will be allowed to be presented or published in any form, by the Investigator or any other person, without the prior written approval of the Sponsor. At the end of the study, a clinical study report will be written by the study Investigators or their designee and reviewed by the Sponsor.

22.0 Amendment to Study Protocol

Two optional study visits have been added to the study protocol. The primary purpose of these visits is to evaluate whether a change in cochlear implant programming, specifically an increase in the number of channels (maxima) will improve subject speech perception in quiet and noise.

These two additional visits will take place at an interval following the 12-month study visit but prior to the 36-month interval. To participate in these additional study visits the subject should have:

Completed the 12-month study visit

Completed the postoperative CT scan per the study protocol

A current MAP with at least 18 active channels, a pulse width of 25 microseconds and a per channel rate of ≤ 900Hz

If a subject is a bilateral CI user, just the first CI will be tested as all testing is done in the unilateral condition – CI alone

If a subject uses hybrid hearing he/she should be tested in the hybrid hearing mode.

22.1 Additional Visit One- Evaluation Details

22.1.1 Hearing History Update

- Document battery usage, preferred listening modality, and changes in tinnitus

22.1.2 Pure tone audiometry

- Frequency-specific thresholds at standard audiometric frequencies for each ear:
    - Air conduction: 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000 and 8000 Hz
    - Bone conduction: 250, 500, 750, 1000, 2000, 3000 and 4000 Hz

22.1.3 Speech Perception Testing using original MAP (<16 maxima)

- CNC Words: Two lists at 60 dBA
    - CI Alone: contralateral ear plugged
- *After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.*
- AzBio Sentences in noise: One list at 65 dBA with a +10 dB and one list at +5 dB signal to noise ratio with speech and noise at 0 degrees azimuth
    - CI Alone: contralateral ear plugged

After completion of testing in noise ask the subject to rank the sound quality on a scale of 1 to 10.

22.1.4 Trans Impedance Matrix Testing (TIM)

The Trans- impedance Matrix (TIM) measurement is a feature in Custom Sound EP, that allows the measurement of the electrical field distribution of each of the intracochlear electrodes with reference to the ECE2 (plate electrode), while either stimulating with reference to the ECE1 (ball electrode) or ECE2 (plate electrode). The intracochlear spread of the electrical fields results in a visual representation which are represented as curves and a heatmap.

22.1.5 Create a new 16 maxima MAP

- Use subject's current preferred MAP parameters and change the maxima to 16. Sound processor configuration should be identical to the original MAP settings

22.1.6 Speech Perception Testing with 16 Maxima MAP

- CNC Words: Two lists at 60 dBA

- CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

- AzBio Sentences in noise: One list at 65 dBA with a +10 dB and one list at +5 dB signal to noise ratio, with speech and noise at 0 degrees azimuth
    - CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

22.1.7 ACE-27 Comorbidity Index

This form documents a subject's comorbidities that may exist with the diagnosis of hearing loss. The form is completed after a thorough review of the subject's medical history.

22.1.8 An anonymized .cdx file will be provided to the study sponsor

22.2 Additional Visit Evaluation Details (Two- Four weeks post Visit One (±2 weeks)

22.2.1 Speech Perception Testing with 16 Maxima MAP

- CNC Words: Two lists at 60 dBA
    - CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

- AzBio Sentences in noise: One list at 65 dBA with a +10 dB and one list at +5 dB signal to noise ratio, with speech and noise at 0 degrees azimuth
    - CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

22.2.2 Speech Perception Testing with Original MAP

- CNC Words: Two lists at 60 dBA

- CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

- AzBio Sentences in noise: One list at 65 dBA with a +10 dB and one list at +5 dB signal to noise ratio, with speech and noise at 0 degrees azimuth
    - CI Alone: contralateral ear plugged

After completion of testing in quiet ask the subject to rank the sound quality on a scale of 1 to 10.

22.2.3 Speech Perception Testing in Noise with Preferred MAP (either original or 16 maxima MAP)

- AzBio Sentences in noise: One list at 65 dBA with a +5 dB signal to noise ratio speech at 0 degrees azimuth and noise at 90 degrees azimuth
    - CI Alone: contralateral ear plugged

22.2.4 Self-Assessment Questionnaire

- The Speech, Spatial and Qualities of Hearing Questionnaire – C (SSQ – C) (Gatehouse & Noble, 2004). The SSQ-C will be used as a subject self-assessment in three categories (speech hearing rating scale, spatial hearing rating scale, and sound qualities rating scale). The SSQ-C is the "comparative" version of the SSQ. The subject will compare their original MAP versus the 16 maxima MAP.

22.2.5 An anonymized .cdx file will be provided to the study sponsor

22.2.6 Retrospective Data Collection: AzBio Sentences in Quiet

AzBio Sentence scores in Quiet for one list at 60 dBA administered; preoperatively and at corresponding post activation interval(s). Intervals to be considered 3, 6 and 12 months. Test conditions of interest are: unilateral aided (ear to be implanted), best aided condition, CI alone and bimodal hearing.

22.3 Adverse Event Reporting

Adverse event reporting for these two additional study visits will include:

- All Serious Adverse Events and
- Adverse device effects and device deficiencies

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22.4 Summary of data collection for two additional study visits

	Visit One	Visit Two
Hearing History	X	X
CNC Words		
Original MAP	X	X
16 maxima MAP	X	X
AzBio Sentences +10 S_0N_0		
Original MAP	X	X
16 Maxima MAP	X	X
AzBio Sentences +5 S_0N_0		
Original MAP	X	X
16 Maxima MAP	X	X
Sound Quality Rating		
Quiet	X	X
Noise	X	X
AzBio +5 S_0N_{90} with preferred MAP		X
SSQ-C		X
Cdx file	X	X
TIM	Either Visit 1 or 2	
ACE-27	Either Visit 1 or 2	
Retrospective: AzBio Sentences in Quiet	Either Visit 1 or 2	

AE reporting (as described in section 22.3)	X	X

23.0 References

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24.0 Change History

Version	Change	Author	Date
1.0	Introduction of document	[redacted]	November 18, 2016
2.0	FDA response to protocol deficiencies. Changes include a glossary explaining the listening conditions for testing and additional inclusion criteria.	[redacted]	December 8, 2016

Version	Change	Author	Date
3.0	Consistent air conduction testing across test sessions, and inclusion of optional preoperative CT scan.	[redacted]	February 1, 2017
4.0	Consistent air conduction testing across test sessions, and inclusion of optional preoperative CT scan. Removal of Cone CT that was included in V3.0. 4.0 sent to FDA as a 5 day notice	[redacted]	February 1, 2017
5.0	Increase # of sites from 10 to 15 and corrected summary table	[redacted]	May 15, 2017
6.0	Removal of investigational for the Nucleus 7 Sound Processor MVBT is now available for use Change in the name of the Chief Medical Officer Inserted that if a site requires assistance with data entry, a non-study staff member would be assigned by the Sponsor to provide the assistance	[redacted]	August 8, 2017
7.0	Addendum to the study protocol to include two additional study visits occurring after the 12 month study interval.	[redacted]	June 28, 2019

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Appendix A: Procedural considerations

- All pre and postimplantation testing will be completed using an audiometer, such as a Grason Stadler GSI 61 (Grason Stadler, Inc., Milford, NH, U.S.A.) or equivalent, calibrated to American National Standards Institute (ANSI) standards with maximum output for frequencies of 0.5 to 4 kHz of no less than 120 dB HL.

- Speech and hearing evaluations will be completed in, at a minimum, a single-walled sound booth capable of accommodating a calibrated, 90-degree, speaker orientation.

- Stimuli will be administered using either insert earphones and/or sound field speakers. Applicable ANSI standards are: ANSI/ASA S3.6-2004; **ANSI S3.1-1999** (R 2003).

- Pure tone threshold exploration will be completed using the adaptive Hughson & Westlake procedure (1944).

- Sound field calibration will be completed as recommended by Katz (2002). The sound level meter should be set to the “A scale” and “slow” settings. The sound level meter will be placed in the center of sound booth, approximately 1m from the loud speaker face, at the height of which would represent the center of an average subjects head. The calibration noise (test specific, however preferably speech spectrum noise) will be administered through the audiometer output to the loud speaker within the sound booth. The sound level meter detects the audiometer output through the loud speaker. With the VU meter on the audiometer set to 0 while, the dial on the audiometer is adjusted until the sound level meter within the sound booth detects the desired output.

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Appendix B: Hearing Aid Fitting Guidelines

Step 1 Create Hearing Aid Program

Method:

1. Using the hearing aid software, create a hearing aid program using the recipients' audiogram.

Step 2 Obtain Real Ear Unaided Response

Method:

1. Calibrate the probe tube.
2. Position the patient one meter in front of the speaker.
3. Place the probe tube in the ear canal approximately 25 to 30 mm past the tragal notch.
4. Select recorded speech at conversational level, 65 dBSPL.
5. Ensure the cochlear implant sound processor is turned OFF.
6. Using the NAL prescriptive algorithm (NAL-NL1 or NAL-RP), obtain REUR.

Step 3 Obtain Real Ear Aided Response

Method:

1. With the probe tube in place, insert the hearing aid. Ensure that it is ON and detected by the hearing aid software. Ensure the cochlear implant sound processor is turned OFF.
2. Select recorded speech at conversational level, 60 dBSPL.
3. Allowing for subjective report, adjust hearing aid software to match real ear target gain and maximum output.

Step 4 Balance hearing aid and cochlear implant loudness

Method:

1. With the hearing aid connected to the hearing aid software, turn the cochlear implant sound processor ON.
2. Select recorded speech at conversational level, 60 dBSPL.
3. Ask the patient to point to which side is loudest or if the sound is balanced.
4. Use the conversational recorded speech to adjust the gain in the hearing aid software as needed to balance the loudness the between the two devices.
5. Repeat for soft speech (50 dB SPL).
6. Adjust the compression ratio and/or compression threshold in the hearing aid as needed so that soft speech is audible and equal in volume.
7. Repeat for loud speech (85 dB SPL).
8. Adjust the maximum power output of the hearing aid as needed so that loud sounds do not exceed the patient's loudness discomfort level.