Cochlear

PROTOCOL

Safety and Efficacy of the Cochlear™ Nucleus® CI422 Cochlear Implant in Adults

Clinical Study

CAM-CI422-2012

FDA Version 4.0

October 2014

Study Sponsor:

Cochlear Americas

13059 E. Peakview Avenue,

Centennial, CO 80111

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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, “Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults.”

Clinical Investigational Site
Primary Investigator’s Name (print)
Title
Signature
Sponsor Representative
Title
Signature

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Table of Contents

Cochlear

Clinical Investigational Synopsis

Title	Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults
Study Sites	Up to 20 North American centers
Study Duration	24 to 36 Months
Study Time	12 months postactivation for each subject
Study Population	Up to 55 postlingually deafened adult subjects
Design Overview	The study will be conducted as a prospective, multicenter, repeated-measure, single-arm, open label clinical study.
Primary Objective	To evaluate the safety and efficacy of the Cochlear™ Nucleus® CI422 cochlear implant for newly implanted adults with expanded indications for candidacy.
Study Intervals	Preoperative Candidacy Assessment Preoperative Baseline Evaluation Surgery Initial Activation 3 Month Postactivation Evaluation 6 Month Postactivation Evaluation 12 Month Postactivation Evaluation
Primary Safety Endpoint	Report of medical/surgical and device related adverse events compared to the current approved labeling with regard to type, frequency and seriousness at 6 months postactivation.
Primary Efficacy Endpoint	Report of clinical performance using an open set monosyllabic word recognition measure at 6 months postactivation.

Glossary

Term	Definition
Best Bilateral Listening Condition	Best postoperative bilateral listening condition referring to either Bimodal or Combined Stimulation (defined below).
Best Unilateral Listening 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**
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**

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**
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 + HA**
Signal-to-Noise Ratio (SNR)	The relationship of the target (signal) to the noise (e.g., if the target speech is 60 dB and the noise is 50 dB then the SNR = +10 dB).

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1.0 Introduction

Cochlear Limited recently launched the Cochlear Nucleus CI422 cochlear implant for commercial distribution in the U.S. The CI422 electrode design combines features of previous generation implants as shown in Figure 1. The design utilizes an optimal insertion angle and cochlear coverage similar to the Contour Advance electrode (P970051/S28), and the thin diameter of the electrode array from the investigational Hybrid clinical trials (G070191) to promote preservation of cochlear structures (Skarzynski et al, 2010; Mukherjee et al, 2012). To date, it has been used successfully in Europe and the United States for patients with a range of hearing losses. Based on positive results in the traditional cochlear implant population (Skarzynski et al, 2012), as well as early reports of success with this electrode in a population with residual hearing (Lesinski-Schiedat et al, 2011; Skarzynski et al, 2012), the Sponsor believes the Cochlear Nucleus CI422 cochlear implant should be formally studied for safety and efficacy in adults with expanded indications for candidacy.

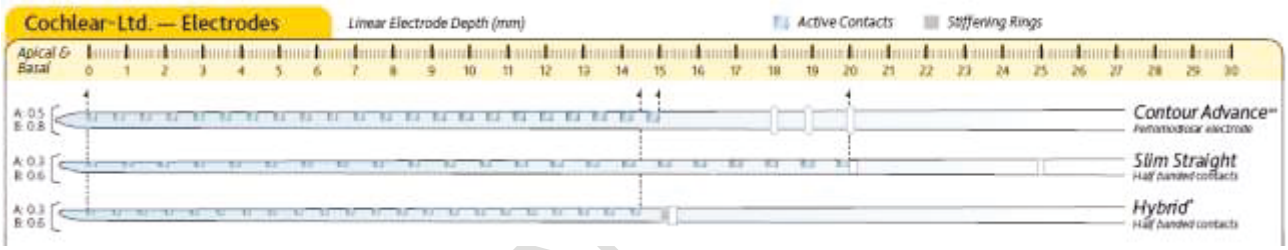


Figure 1. Electrode Comparison Chart

2.0 Study Objective

To evaluate the safety and efficacy of the Cochlear Nucleus CI422 cochlear implant for newly implanted adults with expanded indications for candidacy, using performance on an open set monosyllabic word recognition measure at the 6 month postactivation visit as primary efficacy endpoint.

2.1 General

The Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults study will be conducted as a multicenter, prospective, open label, single-arm clinical study, evaluating the safety and efficacy of the Cochlear Nucleus CI422 cochlear implant in adult subjects with expanded indications for candidacy. A single-subject repeated-measures analysis will be employed whereby subjects will act as their own control.

2.2 Study Design Considerations

A single-subject research design is appropriate since it 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 from device recipients and/or clinical Investigators.

To minimize order effects and test bias, word and sentence lists assigned to the various test conditions will be randomized across conditions, and the order in which test conditions are completed will be randomized.

2.3 Study Procedures

Subjects will be assessed for study purposes preoperatively as well as at intervals corresponding to the initial activation of the device, 3 months postactivation, 6 months postactivation, and 12 month postactivation. Preoperatively, candidates will be assessed in the unaided and aided (i.e., with appropriately fit hearing aids) conditions to determine their candidacy for inclusion into the study. Once determined a candidate, a preoperative baseline evaluation will be conducted to establish baseline measures. Postoperatively, Best Unilateral and Best Bilateral conditions will be tested to evaluate performance with the CI422 implant. The test interval for the primary endpoint of the study for device safety and efficacy is the 6-month postactivation evaluation. Non-study follow-up evaluations may also take place at the discretion of the study site as part of routine care.

2.4 Study Length

It is expected that subject participation will involve a 15 to 18 month commitment, allowing for candidacy assessments, preoperative baseline evaluations, implantation of the device, and postoperative testing.

3.0 Device Description

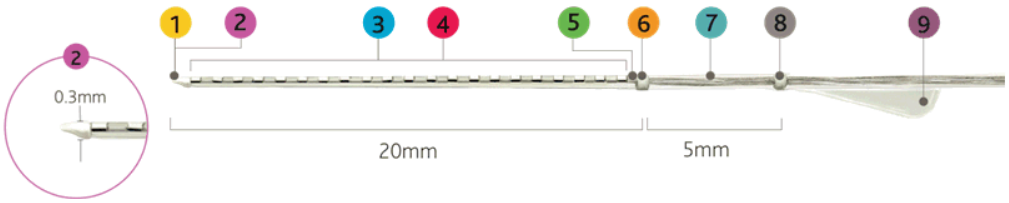
The Cochlear Nucleus implant system proposed to be studied comprises:

- The Cochlear Nucleus CI422 cochlear implant,
- The Cochlear Nucleus 6 (CP900 series) sound processor,
    - Optional acoustic component for any individual with aidable hearing postoperatively
    - Cochlear Nucleus CR210 Remote Control
    - Cochlear Nucleus CR230 Remote Assistant
- The Cochlear Nucleus Custom Sound CS4 programming software.

3.1 Implant Description

The commercially available Cochlear Nucleus CI422 cochlear implant (P970051/S064), as shown in Figure 2, will be used in this study. It incorporates a titanium-cased receiver-

stimulator and a half banded, thin, straight lateral wall electrode array. The array has 22 electrodes spread over 20 mm and an anticipated insertion depth of 20 to 25 mm. The electrode diameter ranges from 0.3 mm (at the tip) to 0.6 mm, with a stiffened basal section designed to minimize lateral wall forces and prevent electrode array buckling. A surgical handle is attached opposite of the electrode contacts to assist with electrode orientation. The resultant typical insertion depth angle is approximately 360°-450° in the scala tympani.



1. Softtip for minimal insertion trauma.
2. Diameter at apical end 0.3 mm.
3. Half-band intracochlear electrode array with smooth lateral surface.
4. 22 platinum electrode contacts spread over 20 mm active length, face medially on opposite side to handle.
5. Diameter at basal end: 0.6 mm.
6. White marker at 20 mm indicates active electrode array.
7. Patented basal stiffener enables smooth, single motion insertion and prevents buckling.
8. White marker at 25 mm indicates maximum insertion depth.
9. Handle assists with reliable electrode orientation and surgical handling.

Figure 2: Characteristics of the Cochlear Nucleus CI422 Electrode

3.2 Sound Processor Description

The Cochlear Nucleus 6 (CP900 series) sound processor (submitted under 970051/C096) as shown in Figure 3, is a behind the ear sound processor with a modular design that incorporates a main signal processing module (the “sound processor”) with built-in directional microphones, a battery module (2-zinc air or rechargeable), radio frequency (RF) coil and coil cable.

Figure 3. Cochlear Nucleus 6 (CP900 series) Sound Processor

The Cochlear Nucleus 6 (CP900 series) sound processor can be programmed to provide electrical stimulation alone for patients with a total loss of acoustic hearing following implant surgery, or to provide both electrical and acoustic stimulation to cochlear implant recipients with postoperative audiometric thresholds between 125 and 2000 Hz measured within an aidable range (defined as air conduction thresholds up to 90dB HL).

3.2.1 Acoustic Component

For recipients with postoperative audiometric thresholds up to 90dB through 2000 Hz, acoustic amplification can be delivered via an acoustic component which connects to the sound processor via a cable molded into the earhook of the speech processor, thereby delivering acoustic amplification in a similar way to a conventional hearing aid (Figure 4). The acoustic component is made up of the EAC200 Series Earhook and the EAC200 Series Power Speaker Unit that is worn in the ear. The Power Speaker Unit is fitted with a choice of instant-fit disposable domes. A choice of two customized hard earmolds may also be available for any subject experiencing fit or comfort issues with the disposable domes.

Figure 4. Acoustic Component Option for the Nucleus 6 (CP900 series) Sound Processor

3.2.2 CR210 Remote Control Description

The CR210 Remote Control (PMA 970051/C096) as shown in Figure 5, is a compact wireless remote device with two-way telemetry that allows the user to make limited changes to the sound processor (e.g., volume, sensitivity, telecoil, and listening programs).

Figure 5. CR210 Remote Control

3.2.3 CR230 Remote Assistant Description

The CR230 Remote Assistant (PMA 970051/C096) as shown in Figure 6, is a slightly larger wireless remote device that contains all of the functional capabilities of the CR210 Remote Control, as well as providing additional processor status information and troubleshooting assistance to the user similar to the commercially available CR110 Remote Assistant (PMA 970051/S049).

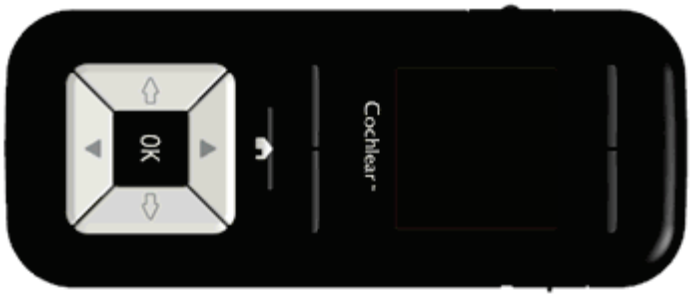


Figure 6. CR 230 Remote Assistant

3.3 Programming Software Description

Programming of the sound processor is achieved via Cochlear Nucleus Custom Sound 4 (CS4) software, which is a modification of the existing, approved, Custom Sound software CS3. Cochlear Nucleus Custom Sound 4 software permits the characterization of both electric and acoustic parameters required for Hybrid simulation as in Custom Sound 2.1 (G070191). The general approach for the electric programming is the same as for traditional cochlear implant recipients except that the software provides more flexible frequency boundary assignments for the 22 channels of the Cochlear Nucleus CI422 cochlear implant. The software provides the ability to specify the cut-off frequency at which acoustic stimulation ends (e.g., thresholds greater than 90 dB HL) and electric stimulation begins. In addition, the software provides a user interface for the clinician to program amplification characteristics (gain and maximum output, frequency by frequency) for the low-frequency range of hearing, from 125 to 2000 Hz.

4.0 Subject Population

Cochlear Americas expects to implant up to 55[1] subjects at up to 20 North American cochlear implant centers. The duration of the multisite study is expected to be up to 3 years, depending on subject recruitment. Other than meeting the inclusion criteria below, subjects will be recruited into the study sequentially to ensure a subject pool representative of the general adult population of those with hearing loss, with no pre-selection based on age (other than being an adult, 18 years-of-age or older), ethnicity or gender.

Prior to recruitment of any subjects into the study, written approval of the investigational plan including clinical protocol and informed consent form will be obtained from the FDA and reviewing Institutional Review Board (IRB).

To be included in the study, subjects must meet the criteria below.

[1] Sample size justification is provided under 8.2 Sample Size; number includes 10% allowance to account for possible subject attrition.

4.1.1 Inclusion Criteria

1. Eighteen years of age or older at the time of implantation
2. Moderate low frequency thresholds up to and including 1000 Hz, severe to profound high frequency (above 3000 Hz) sensorineural hearing loss.
3. Minimum of 30 days experience with appropriately fit bilateral amplification, fit using the standardized NAL fitting method described in the *Fitting and Use of Hearing Aids* section below
4. Aided CNC word recognition score (mean of two lists) between 10% and 50%, inclusive (i.e., 10% ≤ score ≤ 50%), in the ear to be implanted
5. Aided CNC word recognition score (mean of two lists) in the contralateral ear equal to, or better than, the ear to be implanted but not more than 70%
6. Willingness to use bimodal stimulation (i.e., a cochlear implant on one ear and a hearing aid on the contralateral ear) through at least 6-months postactivation
7. English spoken as a primary language

4.1.2 Exclusion Criteria:

1. Duration of severe-to-profound hearing loss greater than 30 years
2. Congenital hearing loss (for the purpose of this study, onset prior to 2 years-of-age)
3. Medical or psychological conditions that contraindicate undergoing surgery as determined by the Investigator
4. Ossification or any other cochlear anomaly that might prevent complete insertion of the electrode array
5. Conductive overlay of 15 dB or greater at two or more frequencies, in the range 500 to 1000 Hz
6. Deafness due to lesions of the acoustic nerve or central auditory pathway
7. Absence of cochlear development
8. Diagnosis of auditory neuropathy
9. Active middle-ear infection
10. Tympanic membrane perforation in the presence of active middle ear disease
11. Unrealistic expectations on the part of the subject, regarding the possible benefits, risks, and limitations that are inherent to the surgical procedure(s) and prosthetic devices as determined by the Investigator
12. Unwillingness or inability of the candidate to comply with all investigational requirements as determined by the Investigator
13. Additional handicaps that would prevent or restrict participation in the audiological evaluations as determined by the Investigator

5.0 Investigational Procedures

5.1 Subject Identification

To maintain confidentiality, the subject's name 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 consented into the study and will be assigned a unique identifier. A unique alphanumeric code will identify the subject throughout the course of the study. For example, US01-422-0000, 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,
- 422 = an abbreviation for the study, in this case 422 for the CI422 implant,
- 0000 = a unique, numeric study site identification.

5.2 Release of Medical Information

The subject 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.

5.3 Description of Test Measures

5.3.1 Audiometric Thresholds

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 narrow band noise and the standard audiometric technique with the speakers positioned at 0° azimuth relative to the subject's head.

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:

- Air conduction thresholds: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz;
- Bone conduction thresholds:125[2], 250, 500, 750, 1000, 1500, 2000, 4000 Hz;

[2] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

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.

- Aided thresholds at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000[3] Hz;
- Tympanometry in each ear

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

The CNC Word Test (Peterson & Lehiste, 1962) is a validated test used clinically and in research to assess the performance of adults with hearing aids or cochlear implants on open-set word recognition. The test consists of 10 recorded lists of 50 monosyllabic words in CD format. For this study, two lists will be administered in quiet at a level equal to 60 dBA in the sound field and scored as total number of words correct, which will be expressed as a percentage correct for this study. Subjects will be tested using a configuration of speech at 0º azimuth in quiet.

5.3.3 AzBio Sentence Test

The AzBio Sentence Test (Spahr et al, 2012) is a validated test used clinically and in research to assess the open-set sentence recognition in speech-spectrum noise of adults with hearing aids or cochlear implants. It consists of 15 lists of 20 sentences each. AzBio sentences are spoken by different talkers in a conversational style with limited contextual cues that the listener can use to predict or 'fill in' unintelligible words. The sentences will be presented at a fixed level in speech weighted noise at a fixed signal-to-noise ratio. Each list includes 5 sentences from 4 different male and female speakers. The average level of intelligibility of each list is 85% +/- 1%. Each word in the sentence counts towards the overall score. Subjects will be tested using a configuration of speech at 0º and noise at 90º/270º azimuth.

5.3.4 University of Washington Clinical Assessment of Music Perception (UW-CAMP) – Pitch Perception Subtest

The UW-CAMP (Nimmons et al., 2008) is a validated test consisting of 3 subtests, designed to provide an assessment of fundamental auditory skills important for music perception. The subtest used in this protocol provides an assessment of pitch perception. Gfeller et al, (2007) illustrated that the presence of low-frequency acoustic hearing improves pitch discrimination in cochlear implant recipients - therefore it is relevant to examine potential changes in performance on this task in subjects with pre-implant low frequency hearing. The UW-CAMP will be presented at 65 dBA. Subjects will be tested using a configuration of 0º azimuth.

5.3.5 Glasgow Benefit Inventory (GBI)

The GBI subject questionnaire is an 18-item postintervention questionnaire, developed for use in otorhinolaryngological (ORL) interventions (Robinson et al., 1996), which assesses

[3] Many audiometers are not calibrated for testing at 6000 and 8000 Hz.

the interventions effects on the health status of patients. "Health status" is the general perception of well-being, including total psychological, social, and physical wellbeing. It can be completed either in an interview or filled-in by the subject. The GBI was designed to be patient-oriented, to be maximally sensitive to ORL interventions, and to provide a common metric to compare benefit across different interventions.

5.3.6 Device Use Questionnaire (DUQ)

A Sponsor designed device usability metric, the DUQ will be administered to determine subjective preferences with regards to device use in various music listening and telephone use situations.

5.3.7 Speech Spatial and Quality-Benefit (SSQ-B) Scale

The SSQ (Gatehouse & Noble, 2004) scale is comprised of 49 questions designed to measure self-reported auditory disability in various listening situations. Its questions cover many aspects of speech perception, spatial hearing, and more general qualities of hearing, such as listening effort. The benefit version of the SSQ (SSQ-B) uses these questions to directly measure the benefits offered by a hearing intervention - in this case cochlear implantation – compared to performance before the intervention was applied (with bilateral hearing aids).

5.4 Preoperative Procedures (within-90 days prior to surgery)

The preoperative assessment will be composed of two evaluations.

- Preoperative Candidacy Evaluation will be completed to determine if the candidate meets the inclusion and exclusion criteria to qualify for enrollment in the study. The Informed Consent form must be signed prior to any study related evaluation taking place.
- The Preoperative Baseline Evaluation will be completed to establish baseline measures after candidacy has been determined. Information gathered during these preoperative procedures will be reported on the appropriate case report forms (CRFs[4]). There will be no predetermined time period required between candidacy and baseline measures. However, candidacy must be re-assessed if more than 90 days have elapsed prior to the surgery date[5].

[4] May be a hardcopy or electronic CRF (eCRF), depending on EDC accessibility at the study site.

[5] If it is more than 90 days past the date of the Candidacy Evaluation, candidacy needs to be re-confirmed by repeating aided CNC word recognition test measures. If a patient experiences a 10% or greater decrement in their word recognition scores, audiometric thresholds must be re-assessed to confirm continued candidacy. Scores from the most recent test session will be used for analysis. If a patient experiences less than 10% decrement in CNC word recognition, the evaluation does not need to be repeated and scores from the initial candidacy/ baseline assessment can be utilized. Any changes observed will need to be reviewed in consultation with the Sponsor prior to surgery occurring.

5.4.1 Preoperative Candidacy Evaluation

5.4.1.1 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 and, along with the results of the preoperative candidacy evaluation, reviewed and approved by Cochlear Americas, as evidenced by the return of a study approval form signed by a Cochlear Americas representative.

5.4.1.2 Fitting and Use of Hearing Aids

Preoperatively, subjects will undergo candidacy testing using their own hearing aid devices. If a candidate does not own hearing aids, testing using loaner hearing aid devices may be provided by the candidate's hearing health provider.

Note: The speech perception criterion for enrollment into the study must be met with appropriately fit hearing aids, (both for the ear to be implanted as well as the non-implant ear), even if amplification proves to provide no measurable benefit over natural acoustic hearing for the particular subject.

To ensure standardization of hearing aid fitting, it is required that hearing aid settings for target and gain are set and verified in accordance with the widely-used National Acoustics Laboratories' (NAL) hearing aid fitting method (Byrne, Parkinson, & Newall, 1990; Dillon, 1999). This widely-used prescriptive hearing aid fitting method, outlined in Appendix C, will use real-ear measures to verify that the slope of the frequency response is within 5 dB per octave of the target slope.

During the fitting process, optimization of the response slope will be the priority for those frequencies where thresholds correspond to aidable hearing. Taking a conservative approach, aidable hearing will be defined by hearing thresholds up to 90 dB HL for this study.

It is recognized that prescriptive methods are based on average requirements, and that individuals may find deviations from target values optimal for sound loudness, quality, or

clarity. For example, individual adjustments required to relieve occlusion effects will be permitted.

If the subject does not use hearing aids on a daily basis, does not own hearing aids, or uses hearing aids that are identified as inappropriately fit or poor functioning, the subject will undergo a hearing aid trial and/or readjustment period with hearing aids that can be programmed to provide appropriate amplification based on NAL fitting method. The hearing aid trial period will be for a minimum of 30 days or longer as recommended by their study audiologist. At the end of the trial period, aided word recognition testing will be assessed to confirm that candidacy criteria are met.

Subjects will need to be willing to use bimodal stimulation (i.e. a cochlear implant on one ear and a hearing aid on the contralateral ear) through at least 6-months postactivation.

5.4.1.3 Candidacy Assessment

- Air conduction thresholds at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz;
    - Unilateral each ear
- Bone conduction thresholds at 125[6], 250, 500, 750, 1000, 1500, 2000, 4000 Hz;
    - Unilateral each ear

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.

- Aided thresholds at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000[7] Hz;
    - Unilateral each ear with contralateral ear plugged
- Tympanometry in each ear
- CNC Word Test – Two lists at 60 dB(A) in each of the following conditions:
    - Unilateral aided each ear with contralateral ear plugged

5.4.1.4 Hearing History and Counseling

Information regarding subject hearing-history (e.g., etiology, onset of hearing loss, duration of severe-to-profound hearing loss, amplification use) will be obtained and reported on the respective case-report form. In addition, patients will be carefully and extensively counseled to ensure that their expectations from cochlear implantation are reasonable and appropriate (as determined by the Investigator).

[6] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

[7] Many audiometers are not calibrated for testing at 6000 and 8000 Hz.

5.4.1.5 Candidacy Determination

Once the candidacy evaluation is completed the Investigator is required to submit the candidacy CRFs for review by the Sponsor's study manager, or designee. The data will be reviewed and candidacy assessed by the study manager. Written approval or disapproval will then be provided by the Sponsor to the Investigator.

5.4.2 Preoperative Baseline Evaluation

Once candidacy has been established, the following additional testing will be administered to each subject:

5.4.2.1 Speech Perception Testing

- CNC Word Test – Two lists at 60 dB(A)
  - Bilateral Aided
- AzBio Sentences in Noise – One list at 65dB(A) with a +5 dB SNR in each of the following conditions
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
  - Bilateral Aided
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in each of the following conditions
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
  - Bilateral Aided

5.4.2.2 Pitch Perception Testing

- UW Camp – Pitch Perception Subtest at 65 dB(A) in each of the following conditions
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
  - Bilateral Aided

5.4.2.3 Questionnaire/Assessment

- Device Use Questionnaire

Note: The Surgical Procedure must be completed within 3 months of the Baseline Evaluation. If the interval exceeds 3 months, candidacy needs to be re-confirmed by repeating aided CNC word recognition test measures. If a patient experiences a 10% or greater decrement in their word recognition scores, audiometric thresholds must be re-assessed to confirm continued candidacy and the Preoperative Baseline Evaluation must be repeated. Scores from the most recent test session will be used for analysis. If a patient experiences less than 10% decrement in CNC word recognition, the evaluation does not need to be repeated and scores from the initial candidacy/ baseline assessment can be utilized.

5.5 Surgical Procedure

The surgical procedure for implantation of the CI422 cochlear implant will be according to current approved labeling as outlined in the surgical manual (P970051/S064). The CI422

Slim Straight Surgical Technique, found in Appendix D, outlines additional considerations and techniques for mitigating the risk of loss of residual hearing for subjects enrolled in this study.

The postoperative hospital stay will be determined by the subject's recovery with surgeon recommendation.

The surgeon is required to complete following each surgery:

- A surgical questionnaire

5.6 Postoperative Procedures

5.6.1 Initial Activation (4 weeks post-surgery, plus or minus 1 week)

5.6.1.1 Audiometric Testing

- Pure tone air-conduction hearing thresholds with insert earphones: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz
    - Unilateral, each ear
- Bone conduction thresholds: 125[8], 250, 500, 750, 1000, 1500, 2000, 4000 Hz
    - Unilateral, each ear

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.

- Tympanometry in each ear

5.6.1.2 Sound Processor Fitting

Threshold (T) and comfort (C) values will be determined for the electrical stimulation for each channel. Impedance telemetry results using common ground (CG) and monopolar (MP1, MP2 and MP1+2) stimulation modes will also be recorded. This information will be used to program the sound processor and also to monitor the device for possible degradation of function and/or damage to neural elements.

For subjects with preserved hearing, the basic programming approach will be to assign frequency channels to the electrode array that supplement the acoustic sensitivity. In other words, the frequency assignment of the electrical stimulation will begin at the frequency where acoustic hearing is no longer useful. For this purpose, hearing thresholds greater than 90 dB will be considered not useful from an amplification perspective and not aidable acoustically. For example, if the subject's hearing in the implanted ear is greater than 90 dB HL for frequencies at and above 1000 Hz, with aidable acoustic hearing up to

[8] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

750 Hz, the lower frequency boundary for electric stimulation will be set as close as possible to 750 Hz (i.e., the last aidable frequency). That is, electrical stimulation will be provided for inputs from around 750 to 8000 Hz and acoustic for frequencies at and below 750 Hz. Map parameters such as rate and maxima will default to clinician judgment of patient preference. An anonymous export of the test map will be sent to the Sponsor.

5.6.1.3 Acoustic Component Fitting

All patients will be fit with the Cochlear™ Nucleus® 6 Sound Processor (CP900 series). In the event that a subject retains aidable hearing, 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 C) to assess the degree to which real-ear targets are met for each subject. Fitting methodology with the Nucleus 6 acoustic component is no different than that of conventional acoustic hearing aids.

Note: For any subject with aidable hearing post-surgery, the acoustic component should be fit. For postoperative testing, the best unilateral condition for the implanted ear will be the Hybrid Mode and the best bilateral condition will be the Combined Mode.

5.6.1.4 Aided Audiometric Testing

- Aided soundfield hearing thresholds: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000 Hz
    - Best unilateral condition, implanted ear with contralateral ear plugged

5.6.2 3 Month Postactivation Evaluation

5.6.2.1 Audiometric Testing

- Pure tone air-conduction hearing thresholds with insert earphones: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz
    - Unilateral, each ear
- Bone conduction thresholds: 125[9], 250, 500, 750, 1000, 1500, 2000, 4000 Hz
    - Unilateral, each ear

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.

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.

[9] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

- Tympanometry in each ear

For this and future visits, any case where previously aidable hearing has worsened and become unaidable between test intervals, this change must be documented on the audiogram for the implanted ear, and further aided and speech testing with the acoustic component should be omitted. The sound processor should be re-mapped to provide appropriate full electric only stimulation to the implanted ear. The subject must use the new electric only program for a minimum of two weeks and return for aided and speech testing at that time. Best unilateral and best bilateral test conditions for that ear at subsequent evaluations will include:

- Electric only, implanted ear with contralateral ear plugged
- Bimodal, bilateral

5.6.2.2 Aided Audiometric Testing

Note: Assessing aided thresholds after the initial activation will only be conducted if there is a shift in unaided hearing of more than 10 dB (for the better or worse) at two or more aidable frequencies.

- Aided soundfield hearing thresholds: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000 Hz
  - Best unilateral condition, implanted ear with contralateral ear plugged

5.6.2.3 Speech Perception Testing

- CNC Word Test (Quiet) – Two lists at 60 dB(A)
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
  - Electric alone condition, implanted and contralateral ear plugged

Note: If the subject lost acoustic hearing in the implanted ear and does not utilize the acoustic component, the best unilateral condition is the same as electric alone and therefore does not need to be evaluated.

- AzBio Sentences in Noise – One list at 65 dB(A) with a +5 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
- AzBio Sentences in Noise – One list at 65 dB(A) with a +10 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition

An anonymous export of the test map will be sent to the Sponsor.

5.6.3 6 Month Post Activation Evaluation

5.6.3.1 Audiometric Testing

- Pure tone air-conduction hearing thresholds with insert earphones: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz
  - Unilateral, each ear
- Bone conduction thresholds: 125[10], 250, 500, 750, 1000, 1500, 2000, 4000 Hz
  - Unilateral, each ear
- Tympanometry in each ear

5.6.3.2 Aided Audiometric Testing

- Aided soundfield hearing thresholds: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000 Hz
  - Best unilateral condition, implanted ear with contralateral ear plugged

5.6.3.3 Speech Perception Testing

- CNC Word Test (Quiet) – Two lists at 60 dB(A)
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
  - Electric alone condition, implanted and contralateral ear plugged

Note: If the subject lost acoustic hearing in the implanted ear and does not utilize the acoustic component, the best unilateral condition is the same as electric alone and therefore does not need to be evaluated.

- AzBio Sentences in Noise – One list at 65 dB(A) with a +5 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
- AzBio Sentences in Noise – One list at 65 dB(A) with a +10 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition

5.6.3.4 Pitch Perception Testing

- UW Camp – Pitch Perception Subtest at 65 dB(A) in each of the following conditions
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition

5.6.3.5 Questionnaires/Assessments

- Glasgow Benefit Inventory
- Speech Spatial and Quality - Benefit

[10] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

- Device Usability Questionnaire

An anonymous export of the test map will be sent to the Sponsor.

5.6.4 12 Month Post Activation Evaluation

5.6.4.1 Audiometric Testing

- Pure tone air-conduction hearing thresholds with insert earphones: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz
  - Unilateral, each ear
- Bone conduction thresholds: 125[11], 250, 500, 750, 1000, 1500, 2000, 4000 Hz
  - Unilateral, each ear
- Tympanometry in each ear.

5.6.4.2 Aided Audiometric Testing

- Aided soundfield hearing thresholds: 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000 Hz
  - Best unilateral condition, implanted ear with contralateral ear plugged

5.6.4.3 Speech Perception Testing

- CNC Word Test (Quiet) – Two lists at 60 dB(A)
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
  - Electric alone condition, implanted and contralateral ear plugged

Note: If the subject lost acoustic hearing in the implanted ear and does not utilize the acoustic component, the best unilateral condition is the same as electric alone and therefore does not need to be evaluated.

- AzBio Sentences in Noise – One list at 65 dB(A) with a +5 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition
- AzBio Sentences in Noise – One list at 65 dB(A) with a +10 dB SNR
  - Best unilateral condition, implanted ear with contralateral ear plugged
  - Best bilateral condition

5.6.4.4 Questionnaires/Assessments

- Glasgow Benefit Inventory
- Device Use Questionnaire

An anonymous export of the test map will be sent to the Sponsor.

[11] Bone conduction measures at 125 Hz are optional based on potential audiometric equipment limitations.

5.7 Summary of Data Collection Visits.

Test	Condition	Preoperative			Postoperative			
		Candidacy	Baseline	Surgery	Activation	3 Month	6 Month	12 Month
Informed Consent		X						
Air Conduction Audiogram	Unilateral Each Ear	X			X	X	X	X
Bone Conduction Audiogram	Unilateral Each Ear	X			X	X	X	X
Aided Audiogram	Hearing Aid Unilateral Each Ear	X						
	Best Unilateral Implanted Ear				X	If >10dB ▲ unaided	If >10dB ▲ unaided	If >10dB ▲ unaided
Tympanometry	Unilateral Each Ear	X			X	X	X	X
CNC words	Hearing Aid Unilateral Each Ear	X						
	Hearing Aids Bilateral		X					
	Best Unilateral Implanted Ear					X	X	X
	Best Bilateral					X	X	X
	Electric Alone					X	X	X
AZBio Sentences In Noise	Hearing Aid Ear to be Implanted		X					
	Hearing Aids Bilateral		X					
	Best Unilateral Implanted Ear					X	X	X
	Best Bilateral					X	X	X
UW Camp Pitch Perception Subtest	Hearing Aid Ear to be Implanted		X					
	Hearing Aids Bilateral		X					
	Best Unilateral Implanted Ear						X	
	Best Bilateral						X	
Surgical Questionnaire				X				
Glasgow Benefit Inventory							X	X
Speech Spatial & Quality-Benefit							X	
Device Use Questionnaire			X				X	X

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6.0 Adverse Events

An Adverse Event (aka Adverse Effect or AE) is the development of an untoward medical occurrence or the deterioration of a pre-existing medical condition following or during exposure to an investigational product, whether or not considered causally related to the product or the surgical procedure to implant it. An untoward medical condition can be symptoms (e.g., nausea), signs (e.g., tachycardia, fever) or clinically significant abnormal results of an investigation (e.g., laboratory findings, chest x-ray).

Adverse events that occur during this study may be associated with the implant procedure, including adverse effects from general anesthesia, or specifically associated with the use of the device. An adverse event will be considered to be device-related when, in the judgment of the Primary Investigator, there is a logical connection between the use of the device and the occurrence of the event, above and beyond the study procedure itself.

A **Serious Adverse Event (SAE)** is any untoward medical occurrence which:

- Results in death;
- Is life-threatening;
- Requires in-patient hospitalization for > 24 hours or prolongation of hospitalization which is not specifically required by the protocol;
- Results in permanent impairment of a body function or permanent damage to a body structure; or
- Requires medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

An **unanticipated adverse device effect** (UADE) is “any 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 (including a supplementary 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)]. The Sponsor will promptly conduct an investigation upon notification by an Investigator of a UADE and will notify the FDA and all reviewing IRBs and participating Investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter, the Sponsor will submit such additional reports concerning the effect as FDA requests.

For the purposes of this study, only unanticipated adverse device effects will be reported to FDA promptly following occurrence. Annual progress reports will contain information regarding SAE/AE occurrences.

6.1 Assessment and Reporting of Adverse Events

6.1.1 Investigator's Responsibilities

Throughout the course of the study, all efforts will be made by the Investigators to remain alert to possible AEs. The first concern will be the safety and welfare of the subject and for providing appropriate medical intervention, as indicated. Detailed information regarding adverse events (AEs) will be recorded by the Investigator at the time an adverse event occurs using an *Adverse Event Questionnair*e, provided as part of the CRFs for the study. All adverse events will be recorded from the day of enrollment (Day 0) to termination of study, approval of the PMA, or when the subject exits the study, whichever is the last, even if the event was acknowledged as a risk factor in the *Informed Consent Form*.

AEs will be recorded on an *Adverse Event Questionnaire* and will include the following information:

- Date of onset
- Date reported to the clinic
- Description of the AE
- Seriousness
- Investigator's assessment of the relationship of the AE to the device and/or procedure
- Treatment
- Outcome

6.1.1.1 Unanticipated Adverse Device Effects

Unanticipated adverse device effects (UADEs) must be reported directly to the clinical center's reviewing IRB and the Sponsor, Cochlear Americas, within 10 working days of knowledge of the event, or as dictated by the specific IRB policy, whichever is sooner. Information regarding the UADE will be recorded on the *Unanticipated Adverse Device Effect Report,* provided with the CRFs for the study*.*

6.1.1.2 Adverse Event Follow-up

All AEs must be followed until resolution, or the condition stabilizes. The Investigator is responsible to ensure that follow-up includes any supplemental investigations as may be indicated to elucidate as completely as possible the nature and/or causality of the AE. This may include additional laboratory tests or investigations, or consultation with other health care professionals. Cochlear or its designee may request that the Investigator perform or arrange for the conduct of supplemental measurements and/or evaluations. AE follow up information will be recorded using a *Follow Up to a Previously Reported Adverse Event Questionnaire,* provided with the CRFs for the study.

6.1.2 Sponsor's Responsibilities

All AEs will be reported annually to FDA in accordance with the IDE regulation [FDA 21 CFR Part 812.150(b)(5)]. All unanticipated adverse device effects (UADEs) will be reported

to FDA within 10 calendar days of the event in accordance with FDA 21 CFR Part 812.46(b) and 812.150(b)(1).

Cochlear Americas or its designee will notify all participating Investigators of any new information that alters the current risk-benefit assessment of the study device or that would be sufficient to consider changes in management of the Nucleus cochlear implant or in the overall conduct of the trial.

6.2 Protocol Deviations

A protocol deviation refers to a study-related activity that is not in compliance with the investigational protocol. Deviations that are required to protect the life or well-being of a subject do not require prior approval from the Sponsor and should be implemented immediately. The IRB and Sponsor must be notified within 5 (five) days of the event.

If a subject is unable to return for follow-up before the closure of a study visit window (+/- 30 days for postactivation study visits), or if protocol defined assessments or parts thereof are omitted or completed incorrectly, the event is to be noted on the Protocol Deviation Log provided to the Investigator in the study Regulatory Binder. Depending on the type or severity of the deviation the Investigator may be required to notify the IRB and/or Sponsor if the deviation impacts safety or performance of the subject or data integrity.

7.0 Study Completion

7.1 Completed Subjects

Each subject in the study will be considered completed when all assessments through 12 months postactivation have been performed in accordance with the study protocol. To be considered a primary endpoint success, subjects must retain their originally implanted device.

7.2 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, reason(s) for discontinuation should be recorded on a study withdrawal form, provided as part of the CRFs 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[12].
- Investigator decision[13].
- Other reason.

In 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, IRB and FDA.

7.3 Premature Study Termination

The Sponsor reserves the right to discontinue the study for any safety, ethical or administrative reason at any time. Subjects already implanted with the device being studied will continue to be supported, independent of any decision made about study continuation.

8.0 Data Analyses

8.1 Study Population

Any subject in whom the Cochlear Nucleus CI422 cochlear implant is attempted to be implanted under this protocol will comprise the intention-to-treat population (ITT). The primary efficacy and safety endpoints will be evaluated with the ITT population. A tipping point sensitivity analysis will be conducted by the methods described in the missing data section to address any missing data.

The effectiveness analyses will also be done on the completed cases (CC) population; treated subjects who had follow-up of the primary endpoint at the protocol prescribed time. A supportive analysis of the primary endpoint will be done in the CC population. Additional analyses will be examined only in the CC population.

8.2 Sample Size

A total sample size of 50 evaluable subjects is planned. An allowance of 10% to account for possible attrition is planned such that up to 55 subjects may be recruited into the study and implanted. The planned sample size of 50 subjects will provide adequate power for the primary efficacy endpoint based on a range of assumptions. Power for this test under

[12] Withdrawal of consent is defined as the subject's voluntary decision to revoke consent to continue participation in the study.

[13] Subject withdrawal from the study is defined as an Investigator decision. The Investigator may elect to withdraw a subject from the study at any time if he/she considers that remaining in the study compromises the patient's health or if the Investigator considers the subject lost to follow-up.

a variety of assumptions is provided below. Calculations are based on a one-sample t-test at a two-sided 0.05 alpha level.

Table 2. Power for Sample Size of 50 Evaluable Subjects

True Population CNC Word Score Mean Change	True Population CNC Word Score Standard Deviation for Change		
	30%	40%	50%
20%	>99%	93%	79%
25%	>99%	99%	93%

8.3 Justification of Pooling Across Study Sites

Pooling data from study sites will be done 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). Maximum enrollment at individual sites will be set at 10 subjects, in an attempt to improve generalizability of the results.

Consistency of the primary efficacy endpoints between sites will be assessed by testing for a difference between sites in the change in CNC word score from preoperative to 6 months postoperative via an analysis of variance model, with the change in CNC word score as the outcome and site as the factor. A p-value for the site factor of less than 0.10 will be considered evidence of differences between sites for the primary efficacy outcome. If there is evidence of a difference, additional analyses will be performed to explore the possible role of baseline characteristics to explain the results. Results for the primary efficacy endpoint will also be presented separately by site, irrespective of the test of differences between sites to help understand both qualitative and non-significant differences between sites.

8.4 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.

In the event a subject is withdrawn prior to the 6-month assessment, the primary analysis of the primary efficacy endpoint will involve imputing the pre-operative CNC word test score for the 6 month CNC word test. This is equivalent to treating each subject with a missing 6 month result as unchanged from baseline. The p-value for the primary efficacy statistical hypothesis test will be calculated using this imputation to understand the impact of missing data on the primary result.

8.5 Additional Statistical Analyses

Statistical Analysis for this study is addressed in detail in the document entitled "Statistical Analysis Plan for the Safety and Efficacy of the CI422 Cochlear Implant in Adults."

9.0 Risk Benefit Statement

It is expected that the risks associated with the procedure to place the cochlear implant are no greater than those associated with cochlear implantation in general. Cochlear implantation is an accepted treatment option for adults with bilateral moderate (for low frequencies) to profound sensorineural hearing loss.

The inclusion criteria for this study allows for subjects to have more hearing preoperatively than current cochlear implant indications for the adult population. It is anticipated that all subjects may lose some or all residual hearing in the ear to be implanted. It is very important for Investigators and subjects alike to understand that this hearing loss is permanent. Audiometric data will be summarized in sufficient detail over the study period to assess any changes in hearing sensitivity. The impact of any such changes will be assessed in light of overall speech perception outcomes. These risks are described in more detail within the patient Informed Consent Form.

Standard length cochlear implantation using the CI422 cochlear implant already provides benefit to adults with bilateral moderate to profound sensorineural hearing loss by restoring the sounds necessary for speech understanding. Due to the characteristics of the CI422 cochlear implant, study subjects who present with hearing outside of currently approved candidacy indications may have the potential to benefit from the use of residual hearing postoperatively. However, implantation using a CI422 cochlear implant means that even if hearing loss occurs, as a direct result of implant surgery or afterwards as a result of natural processes over time, CI422 recipients will have access to full frequency electrical stimulation if needed - without requiring additional surgery. Given the potential for this electrode to deliver significant improvement in the patient's ability to understand speech in quiet and in noise, and to allow for better detection of speech and environmental sounds, cochlear implantation may provide an acceptable risk-benefit to individuals presenting within the expanded indications for cochlear implant candidacy described in this protocol.

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10.0 **Good Clinical Practices Statement**

This trial will be conducted in compliance with all applicable U.S. Federal Regulations pertaining to investigational devices including but not limited to: 21 CFR, Parts 11, 50, 54, 56, and 812 and Good Clinical Practice (GCP) standards. This trial will be conducted in compliance with the protocol as approved by the FDA and each Investigative Site's Institutional Review Board (IRB). Any deviations from the protocol will be reported to the Sponsor and in accordance with the IRB's institutional guidelines.

11.0 **Access to Study Documents and Study Monitoring**

The Sponsor will designate appropriately trained monitors to review the progress of this study and assure the quality and integrity of data accumulated. Clinical monitors, as representatives of the Sponsor, have the obligation to provide site qualification and initiation visits as well as regular site visits. The study monitors will be employees of the Sponsor, Cochlear Americas, or any contracted vendors qualified by experience and training to conduct study site monitoring for this investigation.

Study monitors, employed by Cochlear Americas, for this study will be:

Lori White, AuD
Cochlear Americas
13059 E. Peakview Ave.
Centennial, CO 80111

Aaron Parkinson, PhD
Cochlear Americas
13059 E. Peakview Ave.
Centennial, CO 80111

Kathryn Henion, MA
Cochlear Americas
13059 E. Peakview Ave.
Centennial, CO 80111

Sera Henry, AuD
Cochlear Americas
13059 E. Peakview Ave.
Centennial, CO 80111

All data generated during this study and the source documents from which they originated are open to inspection by the Sponsor or its representative, the FDA, and other regulatory agencies.

Upon completion of the study, the clinical monitor will conduct a final visit, or close-out of the site. The objectives of this visit are to ascertain that all subjects are accounted for, that the regulatory records and reports are complete, verify that study device and other supplies have been accounted for and ensure that the Investigator is aware of his/her responsibilities post-study.

12.0 **Quality Control and Assurance**

Sponsor employees and/or their contracted representatives utilize Standard Operating Procedures (SOP) designed to ensure that clinical study procedures and documentation are consistently conducted/prepared to the highest quality standards. Safety data adjudication will be conducted by the Sponsor's Chief Medical Officer, in accordance with

these SOPs. These SOPs require compliance with federal regulations and Good Clinical Practice guidance.

13.0 **Institutional Review Board**

Prior to the initiation of the study, the Protocol, the Informed Consent Form, and other supporting documentation must be submitted to the Institutional Review Board (IRB) for approval after FDA conditional or final approval. A copy of the IRB approval letter for the Protocol, the Informed Consent, and the Investigator Agreement must be submitted to the Sponsor prior to the consent of the first subject. The study site must maintain an accurate and complete record of all reports, documents, and other submissions made to the IRB concerning this protocol.

A list of the IRB members, their titles or occupations, and their institutional affiliation, or an IRB assurance number and their contact information must be provided to the Sponsor or its designee prior to release of study supplies. Additionally, the Chair of the IRB must be identified.

FDA/relevant health authority regulations require that all advertisements for subject recruitment be approved by an IRB prior to implementation. The complete text and format must be submitted to the Sponsor or its designee for approval prior to IRB submission.

14.0 **Informed Consent Process**

It is the responsibility of the Investigator to inform each subject prior to the initial study evaluation, of the purpose of this clinical trial, including possible risks and benefits, and document the informed consent process in the subject's chart.

A sample informed consent form containing the required elements of informed consent is provided by the Sponsor to each IRB once FDA approved. Any changes made to this sample by the IRB must be approved by the Sponsor, or its designee, prior to final submission to the IRB. After approval by the Sponsor, the final informed consent must be approved by the IRB. Prior to entry into the study or initiation of any study-related procedures, each subject must read, sign, and date the informed consent form. The person executing the consent must also sign and date the consent form. One original informed consent form is to be retained by the study site and a copy is to be given to the subject.

15.0 **Confidentiality**

In accordance with Good Clinical Practices (GCPs) and with the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") all information concerning the subjects in the study must be treated as strictly confidential by all persons involved in the study.

The Investigator acknowledges that any and all information acquired from the Sponsor or its designee or developed or acquired in connection with the study are strictly confidential. The Investigator will not disclose any confidential information to any third party nor use

confidential information for any purpose without first obtaining the consent of Sponsor in writing. Such consent shall be deemed to have been given for disclosure to any person for whom the Investigator is responsible at his/her center, but only so far as required for the purposes of the study, and, in the case of disclosures to staff, only if such staff are bound by obligations of confidentiality no less strict than those set out herein.

16.0 **Protocol Amendments**

The Sponsor will document modifications to the protocol in the form of a written amendment. Amended protocols must be acknowledged by Investigator signature and date upon receipt. Protocol modifications that impact subject safety or the validity of the study must be approved by the FDA and IRB before implementation. In the case of a medical emergency, to remove immediate apparent hazard to subjects, a change may be made preferably after discussion with the Sponsor or its designee. In these instances, the IRB and FDA will be notified as soon as possible.

17.0 **Data Management**

All study data will be entered into an Electronic Database Capture (EDC) system. Study personnel requiring access will have their own Login/Password. Access to clinical study information will be based on an individual's role and responsibilities. The application provides hierarchical user permission for data entry, viewing, and reporting options. For optimum security, all communications between the users and the EDC operate on a secured socket layer (SSL) using 256-bit encryption. The web servers are protected by a managed firewall from potential web and network attacks and the network is guarded by an intrusion detection and protection surveillance system against malicious threats.

This application is designed to be in full compliance with International Conference on Harmonization and Good Clinical Practices (ICH-GCP), FDA CFR 21 Part 11 Electronic Record and Electronic Signatures, the FDA's "Guidance: Computerized Systems Used in Clinical Trials (May 2007), and the Privacy Rule of the Health Insurance Portability and Accountability Act of 1996 (HIPAA)."

As part of the data entry and validation process, the data stored in the EDC is checked against the source data, and also against edit check queries to confirm that the data received is within expected ranges. If any data is missing or is outside of expected limits, a query is created and sent to the site coordinator so that data may be verified and corrected. All changes made to a form are stored in an audit trail.

18.0 **Record Keeping and Retention**

Data generated for the study should be stored in a limited-access file area and be accessible only to representatives of the study site, the Sponsor and its representatives, and FDA/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 kept by the Investigator. This information will be treated with strict adherence to professional standards of confidentiality.

An Investigator must in reasonable time, upon request from any properly authorized officer or employee of FDA/relevant health authority or regulatory agency, permit such officer or employee to have access to requested records and reports, and copy and verify any records or reports made by the Investigator. Upon notification of a visit by the FDA, the Investigator will contact the Sponsor or its designee immediately. The Investigator will also grant Sponsor representatives the same privileges offered to FDA/relevant health authority or regulatory agents/officers/employees.

The Investigator must provide the Sponsor or its designee with the following documents at the time of site qualification and prior to study initiation and retain a copy in the site study file:

- Signed and dated curriculum vitae for the Principal Investigator.
- A copy of the original approval for conducting the study by the IRB. Renewals, with continuance of the study, must be submitted at yearly intervals or as required by IRB policy and a copy of the approved and dated renewal provided to the Sponsor.
- A copy of the IRB approved informed consent form along with any modifications initiated by the Sponsor over the course of the study.
- An IRB member list and Federal Wide Assurance (FWA) Number.
- A signed Financial Disclosure Form for each Investigator.
- An Investigator Agreement for this protocol signed and dated by each Investigator.

In addition to the documents listed above, the study site will also retain the following items and make them available for Sponsor review upon request.

- Certifications, applicable study equipment (audiometers, etc.) calibration records and laboratory reference ranges for all local laboratories used for this study. The Sponsor will verify all equipment requirements at the study qualification and/or initiation. Sites with outdated and/or non-compliant equipment will either not be approved for study participation or will be advised to discontinue study-related activities should non-compliance be noted during regular study monitoring visits.
- All original informed consent forms with required signatures.
- All IRB correspondence (i.e., informed consent [including any approved revisions], protocol, AEs, advertisements, newsletters).
- Copy of the Study Monitoring Log Sheet.
- Clinical and non-clinical supply shipment forms and device accountability logs.
- Copies of all correspondence pertaining to the study between Sponsor and the site.
- Copies of all SAEs reports submitted to the Sponsor.
- Copies of all FDA progress reports submitted to the site by the Sponsor.

- Site Delegation Signature Log.

All study-related records must be maintained for at least 2 years after a marketing application (PMA) is approved for the study device; or if the application is not approved, until at least 2 years after shipment and delivery of the last device for investigational use is discontinued and FDA/health authorities or regulatory agencies have been notified of study closure. The Sponsor will notify the principal Investigator when records are no longer needed. The Investigator will not discard any records without notifying the Sponsor. If the Principal Investigator moves from the current investigational site, the Sponsor should be notified of the name of the person who will assume responsibility for maintenance of the records at the investigational site or the new address at which the records will be stored. The Investigator will notify the Sponsor as soon as possible in the event of accidental loss or destruction of any study documentation.

19.0 **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.

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Cochlear

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.

Cochlear

Appendix B: Instructions for Masking

1. Puretone threshold is established in the test ear.
2. Masking noise is introduced to the non-test ear at the initial masking level (10dB above the established threshold in the non-test ear). Puretone threshold then is re-established.
3. Level of the masking tone or noise is increased subsequently by 5 dB. If there is a response to the tone in the presence of the noise, the level of the noise is increased by 5 dB. If there is no response to the tone in the presence of the noise, the level of the tone is increased by 5-dB steps until a response is obtained.
4. A plateau has been reached when the level of the noise can be increased over a range of 15 to 20 dB without shifting the threshold of the tone. This corresponds to a response to the tone at the same HL when the masker is increased in three to four consecutive levels.
5. Masked puretone threshold corresponds to the HL of the tone at which a masking plateau has been established.

Cochlear

Appendix C: 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.

Cochlear

Appendix D: CI422 Slim Straight Surgical Technique

Electrode specifications:

- Diameter: 0.3 mm at the apical end, 0.6 mm at the basal end.
- Active Length: 20mm; Electrode Length: 25 mm
- The electrode is half banded
- The handle/wing is proximal to the second white marker
- The handle faces opposite to the electrode contacts, and is to remain inferior when inserting the electrode

Pre Incision:

- The patient is prepped and draped in a sterile fashion.
- The incision is marked and the templates are used to mark where the internal receiver/stimulator should be placed.

Surgical Procedure:

- IV steroids may be administered at the discretion of the surgeon as part of standard medical practices. Middle ear steroids or Healon are not recommended for use within this surgical procedure.

- The incision is made and a palva or similar flap is raised to the external auditory canal.

- A pocket is created under the temporal/parietal periosteum to insert the internal device.

- A trough is drilled from the well to the mastoid for the electrode to lie within.

- A mastoidectomy is then drilled with cortical overhangs, followed by the facial recess.

- Once the facial recess is opened, the lip of the round window is drilled away to expose the round window membrane.

- The internal device is secured and the ground electrode is placed under the temporalis periosteum.

A) Specific Round Window Considerations

- Suction is not to be used over the opened round window.
- The electrode is secured prior to its insertion into the cochlea, to facilitate stabilization and orientation of the contacts towards the modiolus.
- A straight incision is be made in the round window membrane with a 22-gauge hypodermic needle, pick or blade.

B) Specific Cochleostomy Considerations

- Suction is not to be used at the cochleostomy site.
- The electrode is secured prior to its insertion into the cochlea to facilitate stabilization and orientation of the contacts towards the modiolus.
- The otic capsule is slowly saucerized using a 1mm diamond burr. The lumen will appear as a bluish or faint gray hue.
- The endosteum is opened using a 0.2mm right angle hook.

Electrode Insertion:

- The Cochlear Nucleus CI422 Electrode is inserted using a smooth, single stroke insertion.
- The electrode is held by the AOS forceps in a parallel fashion. Sharp forceps or an electrode claw are not recommended for use, as they may pinch the active portion of the array.
- The tip of the electrode is guided towards the round window or cochleostomy site by the handle/wing and AOS forceps. The handle/wing is positioned inferiorly during electrode insertion to ensure the electrodes are modiolar facing.
- The electrode is advanced slowly (between 30 to 45 seconds) to limit intracochlear trauma and perilymph displacement. The white markers located at 20mm and 25mm on the array provide a guide of the insertion depth.
- The electrode is inserted to the first point of resistance.
- Once the electrode has been inserted, the cochleostomy site or round window and facial recess is packed.

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults

Instructions to the Investigator:

The investigator must obtain informed consent prior to performing any study procedures. The investigator should keep the original signed consent form, and the subject should be given a copy of the signed document.

Instructions to Potential Subjects:

Please read this consent form carefully. It contains important information to help you decide whether to participate in a research study. The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

This consent form may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand. If you have questions about the research, please consult your doctor or audiologist.

Subject Participation

1. This study involves both inpatient and outpatient care.
2. The Sponsor of this study is Cochlear Americas.
3. The Sponsor plans to enroll a total of up to 55 adult subjects (aged 18 or older) across up to 20 cochlear implant centers in the United States.
4. If you qualify for the study and agree to its requirements, you or your insurance company will be billed for the same cost of a standard Cochlear Nucleus cochlear implant system that would be charged if you were not enrolled in a study.
5. Enrollment into the clinical trial is based upon your candidacy evaluation. You will not be enrolled into the study until that evaluation is complete and shows that you are a good candidate.
6. Before you can start the study, the study doctor or study staff will talk to you about the study. Then you have to sign this consent form before the study doctor or study staff can begin to see if you qualify to be in the study. After you sign this form, the study doctor or study staff will do the things listed below when you come in for study visits. If you would like more information about which tests and procedures will be done at each study visit, ask the study doctor or study staff. Your signature on this Consent Form indicates that you agree to participate in the study entitled “Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults.”

7. Participation requires coming in for up to 2 study visits before the implant surgery, and 4 study visits after the surgery, each of which will take 2 to 5 hours. These study visits will occur across approximately 14 to 16 months. The last visit will occur 12 months after your cochlear implant is activated. Your surgeon or audiologist may require additional follow-up visits as part of your routine care.
8. Cochlear implant device programming and audiology testing will be repeated a number of times during the study visits. You may become tired or bored during these sessions. In order to minimize fatigue, frequent breaks will be offered during the test sessions and/or a test session may be spread across 2 days rather than 1 day.

During the study:

1. You will be evaluated to make sure you are a candidate for the study. Your surgeon will discuss your medical history with you and perform a physical exam. X-rays may be taken of your inner ear(s).
2. You will need to be a bilateral hearing aid user (wear a hearing aid in both ears). You will be required to have a minimum of 30 days experience with well fit hearing aids prior to being accepted into the study. If you already have hearing aids, your audiologist will do a test to make sure they are fit according to a prescription based on your hearing loss. If this test determines that you have been using hearing aids that are not appropriately fit or well-functioning, or you do not own hearing aids, you will need to undergo a minimum 30 day trial period with hearing aids fit to your prescription. Loaner hearing aids may be made available before surgery for *trial* purposes if you do not use hearing aids or need new hearing aids. However, you will be responsible for the cost associated with the fitting of a hearing aid in your nonimplanted ear, if warranted, after surgery. The hearing aid trial, if required, would involve 1 or 2 additional visits to your cochlear implant center.
3. You will need to be willing to use the cochlear implant on one ear and a hearing aid on the opposite ear for at least 6-months following implant activation.
4. Your audiologist will give you a number of hearing and speech tests both with and without hearing aids. These tests will include measuring your ability to hear tones, and to understand speech in each ear. If it is determined that you are a good candidate, your audiologist will do additional testing. The first evaluation may last up to 5 hours, and may be done over 1 or 2 days.
5. Before the cochlear implant surgery, you should discuss the risk of meningitis with your surgeon, and obtain any recommended vaccinations. The Centers for Disease Control (CDC) recommends that persons planning to receive a cochlear implant should be up-to-

date on age-appropriate pneumococcal vaccination ≥2 weeks before surgery, if possible. (More information about the CDC's recommendations can be found at http://www.cdc.gov/mmwr/preview/mmwrhtml/m2e731a1.htm or by calling the CDC's National Immunization Information Hotline at 1-800-232-2522).

6. You will receive a cochlear implant system. A cochlear implant has two parts: an internal part called the implant, and an external part called the speech processor. You cannot see the internal part because it is under the skin. The speech processor sits behind the ear similar to a hearing aid.
7. You will undergo cochlear implant surgery. Cochlear implant surgery requires general anesthesia (going to "sleep"). This surgery normally takes 2 to 3 hours. During surgery, your scalp may need to be shaved around the site of the implant. The surgeon will make an incision (cut) behind your ear, create a pocket in the bone for placing the implant, and thread an electrode array (a very small, thin "tube" of silicone rubber with 22 metal contacts) into the inner ear. Then the incision is closed. The length of the hospital stay will be determined by your surgeon. Typically, implant patients go home later the same day or early the following morning. Most people return to normal activities within a few days or a week. As with any surgery, there may be some discomfort. Most discomfort or pain after the operation can be managed with standard pain-killing medicine.

   If you have questions regarding the surgery, it is important that you discuss them with your surgeon or cochlear implant team before you sign this form.
8. You will be required to wear a hearing aid in the unimplanted ear after surgery, in addition to the cochlear implant system, for a period of at least 6 months. However, if a new hearing aid is required to provide appropriate amplification for the unimplanted ear after surgery, the cost of the hearing aid will be your responsibility.
9. You will return to your cochlear implant center for activation of the cochlear implant system by your audiologist following a healing period (typically 2-to-6 weeks). The length of the healing period will be determined by your surgeon. You will be fitted with a Cochlear™ Nucleus® 6 sound processor (CP900 series). You will be instructed on the system's use and care.
10. You will be required to complete the next 3 sessions within an acceptable time frame based on this initial activation date. Each appointment will be referenced to this date and must not be more than 30 days outside of the specified interval. That means that the "3-month postactivation" appointment must be done 2 to 4 months after the initial activation appointment, the "6 month" appointment must be within 5 to 7 months after the initial activation appointment, etc. It is

very important that you come to all the appointments during the course of the study.

11. At the study visits, before and after the surgery, you will participate in routine hearing testing and speech understanding tests in quiet and when there is background noise. At some appointments you will also be asked to listen for differences in music tones. These visits will each last between 2 and 5 hours.
12. Finally, you will be asked to complete study questionnaires about how the cochlear implant has affected your health and ability to hear in everyday life situations.

Reimbursement and Costs

Being in this study is voluntary. Cochlear will pay you $12.50 per hour for each study visit. The number of hours paid will be based on the amount of time you will spend per session. It will include these measurement sessions: candidacy, baseline, initial activation, 3 months, 6 months, and 12 months postactivation. The Sponsor will pay for your meals during your day of testing. With prior approval, the Sponsor will pay for an overnight hotel stay if you live more than 2 hours away from the clinic for test sessions that will take more than 2 hours to complete, if required. If you would like to receive payment for your participation, you will need to complete a W-9 form that reveals your name and social security information. A W-9 is required because study payments for your time are taxable. This does not apply to payments made to you as reimbursement for meals or any hotel stays. Lastly, you are responsible for, and will have to pay for, transportation to and from your clinic for study visits.

If you agree to participate in this study, please understand that you and/or your insurance company will be billed for a Nucleus cochlear implant system and for surgery. You or your insurance company will be billed for any medical, surgical, or audiology treatment that you might need after receiving the cochlear implant. Cochlear Americas will not pay you for any audiology or medical evaluation conducted before or after surgery. You will not be reimbursed by Cochlear Americas for the surgery, programming of the device, or any therapy you receive. These services are all standard components of learning to hear with a cochlear implant.

Where possible, your own existing hearing aids will be used during the study. However, as stated above, if a new hearing aid is required to provide appropriate amplification for the unimplanted ear after surgery, the cost of the hearing aid will be your responsibility.

It is important that you check with your insurance company about payment for the cochlear implant surgery. It is possible that your insurance company may not pay for a cochlear implant because you have better hearing than most current implant candidates. If your insurance company does not agree to pay for the cochlear implant, you will be billed for the surgery whether or not you

choose to participate in this study.

Purpose and Background

This study involves research. The main purpose of this research is to assess whether the CI422 cochlear implant is safe and effective in people who may have more hearing than current cochlear implant candidates.

The CI422 cochlear implant device was approved on March 26, 2012 by the Food and Drug Administration (FDA) for people who have less hearing than you do. At this time, cochlear implants are not commonly used for people with your type of hearing loss. You are being asked to participate in this research study because, based on positive results in early studies, the Sponsor believes the Cochlear Nucleus CI422 cochlear implant should be studied in more people with hearing loss like yours.

The devices to be used in this study include:

- The Cochlear Nucleus CI422 cochlear implant. The Cochlear Nucleus CI422 cochlear implant is different from previous commercial cochlear implants in that it has a newly designed thin, straight electrode array. The thinner electrode array design is intended to help preserve the delicate structures in the cochlea.
- The Nucleus 6 (CP900 series) sound processor (a mini "computer" that picks up sound with a microphone and converts those sounds into an electric signal).
- An acoustic component, which consists of a mini speaker built into a soft dome earpiece that will fit in your ear. The acoustic component is connected to the sound processor and delivers amplified sound to your ear in the same way that a hearing aid does. This component will be used in combination with the sound processor if any low pitch hearing is present after your cochlear implant surgery.

The sponsor expects that you will lose some or all residual hearing in the implanted ear at the time of cochlear implantation. The sound processor will be adjusted to match your hearing profile after surgery.

In summary, this study will look at whether or not the CI422 cochlear implant works as well or better than a hearing aid for providing speech understanding to people with your type of hearing loss.

Possible Benefits from the Research

The Cochlear Nucleus CI422 cochlear implant with Cochlear Nucleus 6 sound processor system may improve your understanding of speech in quiet and in noise. The implant also may enable you to hear sounds in your environment better than you do now.

If any low pitch hearing is present after your surgery, the combination of low-pitched acoustic (via amplification) and high-pitched electric hearing from the cochlear implant may provide you with additional speech understanding in

quiet and noise. It is also possible that the addition of acoustic hearing from the other ear (via a hearing aid) will provide further benefit.

The information gained from your participation in the study will provide useful information to Cochlear Americas, the distributor of the device, which may benefit future cochlear implant recipients with hearing loss like yours.

It is important to understand that these are possible benefits. There is no way to know for sure that you will have these or any benefits from the cochlear implant. It is possible that there may be no benefit to you from joining this study.

Possible Risks from the Research

Risks Associated with All Surgery

a) Risks associated with ALL surgery include the possibility of pain, scarring, bleeding and infection after surgery.

b) The use of anesthesia has inherent risks to the heart, lungs, kidneys, liver and brain and, in rare cases, can result in death.

Risks Associated with All Ear Surgery

a) Risks associated with ALL ear surgery include potential damage to the facial nerve and dizziness. This procedure may result in infection or bleeding, or numbness or stiffness about the ear. Taste disturbance, increased tinnitus, neck pain, skin reactions, and leakage of inner ear fluid are possible risks. Facial nerve monitoring will be performed during the implant surgery. Before your surgery, your ear surgeon and anesthesiologist will discuss with you the risks of cochlear implant surgery.

b) Meningitis is a known risk of inner ear surgery. Meningitis is an infection. The infection is in the fluid and tissue that surrounds the brain and spinal cord. There are two main types of meningitis, viral and bacterial. Bacterial meningitis is the most serious type. It is the type that has been reported to occur in some people with cochlear implants. Certain conditions may increase the risk of meningitis. These conditions include congenital ear malformations, the presence of a cerebral spinal fluid (CSF) shunt or drain, recurrent episodes of bacterial meningitis prior to cochlear implant surgery, the presence of a perilymphatic fistula, and some types of skull fractures and defects.

Risks Associated With All Cochlear Implant Surgeries

Risks associated with implantation of the internal receiver-stimulator and cochlear electrode array include:

a) Failure of parts of the implanted device could result in removal, replacement of the implant, or a reduction of the number of electrodes in use. The risk of removing a failed implant, if necessary, is thought to be small. An implant

may be removed and replaced with another device.

b) Failure of the operation, perhaps requiring removal of the implant.

c) Irritation, redness or breakdown of the skin in the area around the receiver-stimulator and /or rejection of the device. The electrode array may migrate (move) partially, resulting in decreased hearing ability. The electrode array may perforate structures of the external or middle ear, such as the eardrum or canal wall. Misplacement of the electrode may result in nonauditory sensations. Such complications may require additional medical treatment, surgery and/or removal of the device.

d) Increased tinnitus or facial nerve stimulation due to the electrical stimulation of the implant. This could also cause dizziness or pain.

e) Component failure may reduce the number of electrodes available for programming and may result in the perception of uncomfortably loud sounds or no sound.

f) Loss of any remaining hearing in the ear that will receive the cochlear implant.

Please see Appendix A of this form for the full list of warnings for people who receive a cochlear implant.

Risks Specifically Associated With This Trial

You will likely lose at least some hearing in the ear that is implanted. It is possible that you will lose all hearing in this ear. Even if you do not lose hearing right after surgery, it is possible that there could be a gradual or sudden hearing loss at any time. If you notice any change to your hearing, even if you believe that it is related to your hearing aid or sound processor, it is important that you seek immediate medical attention to assess whether treatment is needed.

It is important to understand that a loss of residual hearing is permanent and it may in some cases result in more difficulty hearing in everyday listening situations. For example, with your cochlear implant and hearing aids off, hearing your own voice or detecting environmental sounds (such as the doorbell or the telephone ringing) may be more difficult. A loss of low pitch hearing in your implanted ear may cause you to have more difficulty in locating the direction of a sound in the environment, or identifying a telephone caller as male or female.

Speech and other sounds will not sound the same through your implant as they did before you lost your hearing, and may take some time to adjust to. If any low pitch hearing is present after your surgery, there might be some risk of interference between the electrical hearing you receive from the cochlear implant and your low pitch hearing. This might be all the time or sometimes. Any interference you might experience is expected to go away if you turn the cochlear implant processor off. Even if it is difficult at first to listen with the cochlear implant, it may become easier over time as you gain experience listening with it. If you do not benefit from the cochlear implant or do not like

listening with it, you can stop using the device by not using the speech processor. If you decide the implant is not useful you will be provided with information about other options such as using hearing aids.

There is a risk of mild irritation of the ear-canal by hearing aid earmolds or the ear piece of the acoustic component.

There may be other, unknown or unforeseen side effects as part of this clinical trial.

Participation is Voluntary

Participation in any research project is voluntary. If you do not wish to take part you are not obligated to. If you decide to take part and later change your mind you are free to withdraw from the project at any stage. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you, or your relationship with your clinic.

Alternatives to Participating in the Research

You may decide not to participate in this clinical study. You may continue to use hearing aids. You may elect to use transposition hearing aids, which are specifically designed to superimpose high-pitched information onto regions of lower pitch hearing that remain usable. You may choose to receive specialized training to improve speech-reading and listening skills. These options do not require surgery.

Compensation for Injury

You may develop medical complications from participating in this study. If this happens, the study staff will provide emergency medical treatment and will assist you in obtaining appropriate medical treatment. However, there are no plans to provide compensation or reimbursement for such treatments or for any additional costs – medical or otherwise.

In case of injury as a result of this clinical investigation: <insert institution> will provide immediate medical treatment in the event that a physical injury results because of your participation in this research study. You will be billed for the cost of such medical care not reimbursable through your health insurance.

If you experience an injury, immediately contact the investigator:

<insert Investigator Name>

<insert Address>

<insert Phone #>

<insert Email>

Questions and Concerns

Should you have questions or concerns regarding your participation in this research study or if you feel you have experienced a research-related injury, consult the investigator:

<insert Investigator Name>

<insert Address>

<insert Phone #>

<insert Email>

Should you have questions concerning your rights as a research subject, you may contact:

<insert Institution IRB>

<insert Address>

<insert Phone #>

<insert Email>

The Institutional Review Board (IRB) is a group of people who perform independent review of research as required by regulations.

Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The investigator must get your permission to use or give out any health information that might identify you.

What information may be used and given to others?

If you choose to be in this study, the investigator will get personal information about you. This may include information that might identify you. The investigator may also get information about your health including:

a) Past and present medical records

b) Research records

c) Records about phone calls made as part of this research

d) Records about your study visits

e) Information obtained during this research about

i. Physical exams
ii. Study test results
iii. Questionnaires
iv. Records about the study device

Who may use and give out information about you?

Information about your health may be used and given to others by the investigator and staff. They might see the research information during and after the study.

Who might get this information?

Your information may be given to the Sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the Sponsor, or are owned by the Sponsor.

Information about you and your health which might identify you may be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- <insert institution> Institutional Review Board.

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The Sponsor will analyze and evaluate the results of the study. In addition, people from the Sponsor and its consultants will be visiting the research site. They will follow how the study is being done, and they will be reviewing your information for this purpose.

The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the Sponsor can receive marketing approval for new products or candidacy indications resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

The information may be reviewed by <insert institution> IRB, a group of people who perform independent review of research as required by regulations.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above. If you refuse to give permission, you will

not be able to be in this study.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information at any time. If you decide to be in this study you will not be allowed to look at or copy your research information until the study is complete.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

General Conditions

Should you consent to participate in this research, your identity will be kept confidential within specific limits. The U.S. Food and Drug Administration may review your records. In addition, it may be necessary for this consent form and other medical records to be reviewed by representatives of other appropriate regulatory agencies and Cochlear Americas.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

All forms of medical diagnosis and treatment, whether routine or experimental, involve some risk of injury. Despite all precautions, you may develop medical complications from participating in this study. Should such complications arise, the researchers will provide emergency medical treatment and will assist you in obtaining appropriate medical treatment. However, this study does not provide compensation or reimbursements for such treatments or for any additional costs – medical or otherwise.

Your Participation in this Research is Voluntary

You may withdraw from the research project at any stage. Should you decide to participate in this study, and later elect to discontinue, you may withdraw

without penalty or loss of benefits to which you are otherwise entitled. You may withdraw from the study by notifying your audiologist or surgeon.

Additional Information

a. The study may be stopped earlier than anticipated.

b. Any important new findings made during the course of the research will be provided to you. This may affect your willingness to continue in the study.

c. Your participation in this study does not limit any protection or rights you may have pursuant to any applicable federal, state or local laws.

d. Your participation may be ended by the investigator without your consent IF:

- Such participation is shown to be life threatening or hazardous.
- There are unanticipated business, legal or regulatory circumstances that make continuation impossible or commercially impractical.

Release of Information:

I give permission for Cochlear Americas to have access and copying rights to all medical and hospital records concerning my participation in this research. I also authorize Cochlear Americas, the U.S. Food and Drug Administration, and other regulatory authorities to use this information. I, otherwise, do not allow disclosure of any information that is individual or personal to me.

Name of Participant:_____

Signature:_____

Date:_____

Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults

INFORMED CONSENT

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

Agreement to Participate:

I have read and understand the description of the "Safety and Efficacy of the Cochlear Nucleus CI422 Cochlear Implant in Adults" study. I hereby consent to the research as described.

I understand the risks, benefits and alternatives to participation in this clinical trial.

I certify that:

- I am / am not (circle one) participating in another research project at this time.
- I have discussed the implications of such activity, if any, with the Primary Investigator of this project.

In consideration of this understanding, I voluntarily agree to enroll in this research at:

<insert institution>

Print Participant Name	Participant Signature	Date

Print Person Name of Person Obtaining Consent	Signature	Date

Appendix A

Warnings and Precautions for the Nucleus Cochlear Implant

a) Long-term Effects of Electrical Stimulation - - Most cochlear implant recipients benefit from electrical stimulation at levels that are considered safe, based on animal experimental data. For some recipients, the levels needed to produce the loudest sounds exceed these levels. The long-term effects of such stimulation in humans are unknown.

b) Head Trauma - - A blow to the head in the area of the cochlear implant may damage the implant and result in its failure.

c) Ingestion of Small Parts - - The external cochlear implant system contains small parts that may be hazardous if swallowed.

d) Batteries can be harmful if swallowed. Ensure that batteries are kept out of reach of young children. If swallowed, seek prompt medical attention at the nearest emergency center.

e) Scuba Diving- - Recipients of a cochlear implant should seek medical advice before participating in a dive for conditions that might make diving contraindicated, e.g., middle-ear infection, etc. When wearing a mask, avoid pressure over the implant site. Maximum diving depth for the Nucleus cochlear implant is 40 m or 131 feet.

f) Rechargeable Batteries - - In certain circumstances, rechargeable batteries can become VERY HOT, and could cause injury. Rechargeable batteries should NEVER be worn beneath clothing (including scarves and headwear covering the ears). Use of the rechargeable battery is contraindicated in patients who cannot remove the device by themselves, or notify a caregiver that the device has become hot.

g) Sleeping - - Do not wear the sound processor while sleeping, as you may not become aware of your processor becoming unusually warm or hot.

h) Retention aids - - When using retention aids such as the Snugfit™ or LiteWear, be aware that it may take longer to remove the processor if the processor becomes unusually warm or hot. Do not attach the LiteWear beneath layers of clothing.

i) Electromagnetic Interference - - Some types of digital mobile telephones or hand-held communication devices (e.g., walkie-talkies) may interfere with your cochlear implant system. You may perceive distorted sound when you are within 12 feet of such devices. You may experience distorted sound when passing through or near devices such as airport metal detectors and commercial theft detection systems. You may need to turn off your sound processor when near such systems. The system may activate metal detectors. You should

carry the Cochlear Implant Patient Identification Card with you at all times. Sound quality may also be distorted when you are within one mile of a radio or television transmission tower. The effect is temporary and will not damage your system.

Warnings Regarding Specific Medical Treatment:

Some medical treatments generate induced currents that may cause tissue damage or permanent damage to the cochlear implant.

a) Electrosurgical instruments (electric instruments used to cut tissue or bone or stop bleeding) are capable of producing radio frequency currents that may flow through the electrode array. Monopolar electrosurgical instruments must not be used on the head or neck of a cochlear implant recipient, as induced currents could cause damage to cochlear tissues or permanent damage to the implant. Bipolar electrosurgical instruments may be used on the head and neck; however, the cautery electrodes must not contact the implant and should be kept more than 1 cm (about 1/2 inch) from the extracochlear electrodes.

b) Therapeutic or medical diathermy (treatment that involves heating body tissue) using electromagnetic radiation (magnetic induction coils or microwave) must not be used. High electric currents, which may be induced into the electrode array from these procedures, can cause tissue damage to the cochlea or permanent damage to the implant.

c) Neurostimulation (stimulating the brain or parts of the brain with electricity) must never be applied directly over the cochlear implant. High currents induced into the electrode array can cause tissue damage to the cochlea or permanent damage to the cochlear implant.

d) A cochlear implant recipient must not undergo electroconvulsive therapy (shock therapy) under any circumstances. Electroconvulsive therapy may cause tissue damage to the cochlea or damage to the cochlear implant.

e) Recipients of cochlear implants should not undergo ionizing radiation therapy directly over the cochlear implant.

f) Magnetic Resonance Imaging (MRI) is contraindicated except under the circumstances described below. Cochlear implant recipients must not be in the room where an MRI scanner is located, except under the following special circumstances:

- Nucleus cochlear implant system has a removable magnet and specific design characteristics to enable it to withstand MRI up to 1.5 Tesla, but not higher. The cochlear implant magnet must be surgically removed prior to an MRI procedure.
- Cochlear implant recipients must take off the sound processor and headset before entering a room where an MRI scanner is located.

- If the implant's magnet is still in place, tissue damage may occur if the recipient is exposed to MRI. Once the magnet is surgically removed, the metal in the cochlear implant will affect the quality of the MRI. Image shadowing may extend as far as 6 cm from the implant, thereby resulting in loss of diagnostic information in the vicinity of the implant.
- If you need additional information about removal of the magnet, please contact Cochlear Americas.