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IRB Approved at the
Protocol Level
Sep 13, 2018

PROTOCOL

Clinical Investigation of New CI Delivery Models in a Nucleus CI Population

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Version 2.0

August 2018

Study Sponsor

Cochlear Americas

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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, “Clinical Investigation of New CI Delivery Models in a Nucleus CI Population.”

Clinical Investigational Site

Primary Investigator’s Name (print)

Title

Signature

Sponsor Representative

Title

Signature

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1.0 Clinical Synopsis

Investigation title	Clinical Investigation of New CI Delivery Models in an Nucleus CI Population
Total expected duration of the clinical investigation	18-24 months
Enrollment period	Newly implanted subjects (Group 1): up to 12 months Existing subjects (Group 2): up to 6 months
Expected duration per subject	Newly implanted subjects (Group 1): up to 6 months post-activation Existing subjects (Group 2): up to 8 weeks
Investigational design	The clinical investigation will be conducted as a nonrandomized, single-subject, repeated-measures design in which each subject serves as his/her own control.
Number of subjects	Newly implanted subjects (Group 1): Minimum of 30 subjects, up to 50 subjects Existing subjects (Group 2): Minimum of 50 subjects, up to 100 subjects
Number of investigational sites	Up to 10 sites
Inclusion criteria	• Newly implanted and existing recipient Groups (Groups 1 and 2): o Age 12 and older o For Group 1 only: CNC word recognition score administered at 60dBA (2 lists) with an appropriately fit hearing aid in the ear to be implanted, who are receiving a cochlear implant as standard of care o For Group 2 only: 3 months or greater combined experience with Nucleus 5, 6, Kanso, or 7 series sound processor o Fluent spoken English skills
Exclusion criteria	• Newly implanted and Existing Recipient Groups (Groups 1 and 2): o Unrealistic expectations on the part of the subject regarding the possible benefits, risks, and limitations o Additional cognitive, medical or social handicaps that would prevent completion of all study requirements as determined by the Investigational team o Unwillingness or inability of the subject to comply with all investigational requirements o Use of an acoustic component in the implanted ear o Less than 18 active electrodes o Hybrid L Cochlear Implant
Primary objective	Group 1 (Newly Implanted): To compare preoperative speech recognition with an appropriately fit hearing aid to Cochlear Implant (CI) performance at 6 months using a CNC Monosyllabic Word Test administered in soundfield at 60dBA for the implanted ear.

	Group 2 (Existing subjects): To compare performance in subjects using an expert clinician (EC) MAP versus an Artificial Intelligence (AI) MAP after one month experience on a CNC Monosyllabic Word score administered in soundfield at 60dBA.
Primary endpoint	Group 1 (Newly Implanted): Improved group mean CNC word recognition in quiet measured after 6 months of experience compared to the preoperative appropriately fit hearing aid condition in the implanted ear. Group 2 (Existing subjects): Group mean CNC word recognition in quiet will be the same or better with one month AI MAP experience when compared to EC MAP.

Additional analyses	• To characterize clinician satisfaction of the AI system and psychoacoustic tests for both newly implanted and existing subjects
	• To characterize subject satisfaction of the AI system and psychoacoustic tests for existing subjects
	• To characterize performance on psychoacoustic test metrics over time in both newly implanted and existing subjects
	  o Phoneme Discrimination via direct connect
	  o Word Discrimination via direct connect
	  o Loudness Growth via direct connect
	  o Audiogram via direct connect
	• AzBio Sentences in Noise at 60 dBA at +10 dBSNR (S0N0) presented in soundfield
	• CNC Monosyllabic Phoneme score at 60 dBA presented in soundfield

Investigation schedule	**Group 1 Newly Implanted subjects**
	
	Pre-operative Testing
	o Two lists of CNC words in the ear to be implanted
	o Completion of SSQ Questionnaire
	
	Visit A: Initial Activation (2-4 weeks post surgery)
	o Create AI Automaps
	o Clinical counseling
	o Send anonymous CDX file to Cochlear
	
	Visit B: 1 month post Visit A (3 weeks +/ 1 week)
	o Administer psychoacoustic tests:
	  o Audiogram → FOX Initial advice
	  o Phoneme discrimination → FOX Standard advice
	o Program with AI MAP
	o Clinical counseling
	o Send anonymous CDX file to Cochlear

Visit C: 3 months post Visit A (+/- 2 weeks)

- Collect CNC Words and AzBio Sentences presented in soundfield at +10dB SNR presented in soundfield with AI MAP
- Administer psychoacoustic tests via direct connect to include:
  - Speech audiometry
  - Loudness scaling
  - Pending outcome requests (if any)
- Program with AI MAP
- Clinical Counseling
- Send anonymous CDX file to Cochlear

Visit D: 6 months post visit A (+/- 2 weeks)

- Collect CNC Words and AzBio Sentences presented at +10dB SNR in soundfield
- Administer psychoacoustic tests via direct connect to include:
  - Speech audiometry
  - Loudness scaling
  - Pending outcome requests (if any)
- Program with AI MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear
- Completion of SSQ Questionnaire

Group 2: Existing subjects

Visit A

- Collect CNC Words and AzBio Sentences presented at +10dB SNR in soundfield with current MAP
- Administer psychoacoustic tests via direct connect to include:
  - Audiometry
  - Phoneme discrimination
  - Loudness scaling
  - Speech audiometry
- Create AI AutoMAP
- Administer psychoacoustic tests via direct connect to include:
  - Audiometry→ FOX Initial Advice
  - Phoneme discrimination→ FOX Standard Advice
- Create AI take home MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear

Visit B: 1 month post visit 2A (+/- 1 week)

- Collect CNC Words and AzBio Sentences presented at +10dB SNR in soundfield with AI MAP
- Administer psychoacoustic tests via direct connect to include:
  - Pending Outcome Requests*
  - Speech audiometry→ FOX Standard Advice
- Subject questionnaire
- Clinical counseling
- Send anonymous CDX file to Cochlear

	○ Collect CNC Words and AzBio sentences presented at +10dB SNR in soundfield with AI MAP (acute testing of optimized AI MAP)

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2.0 Glossary

Term	Definition
CI	Cochlear Implant
IA	Initial Activation
AE	Adverse Event
IRB	Institutional Review Board
CRF	Case Report Form
SAE	Serious Adverse Event
Direct Connect	Subject evaluation including the Personal Audio Cable outside of the soundfield. Also referred to in separate documents as CoalaLink.
MAP	Individualized listening program created for cochlear implant recipients
AI	Artificial Intelligence: behaves similar to car navigation. Logic based in knowledge, decision making and learning capacity.
Artificial Intelligence (AI) MAP	Map created with AI
Expert Clinician (EC) MAP	MAP created by experienced clinician using traditional methods (subjective T/C levels or NRT based and potential modifications of defaults)
AutoMAP	AI modifications to programming parameters, with similar stimulation compared to EC MAP
Auditory hierarchy skills	Skills to determine auditory processing ability—or listening success. They develop in a general four- step hierarchy, but all work together and are essential for daily listening. These include detection, discrimination, identification and comprehension.
Psychoacoustic tests	This term is an overarching name for the Speech audiometry, phoneme discrimination, loudness scaling, and audiometry collected via Direct Connect. These tests collect data regarding the auditory hierarchy skills through the cochlear implant. Results from these tests are incorporated into recommendations for the AI MAP.
Speech Audiometry	Single word speech test presented at various intensity levels to measure subject performance. This test evaluates auditory identification and comprehension through the cochlear implant after surgery, via direct connect.
Audiometry	Narrowband noise presented at various intensity levels to measure sound audibility. This test evaluates auditory detection of sound through the cochlear implant after surgery, via direct connect.

Phoneme discrimination	Assessment the spectral discrimination capacity of the aided cochlea. Coding spectral differences is the core function of the cochlea. Pairs of speech sounds presented at various intensity levels to measure auditory discrimination and identification at various intensities through the cochlear implant after surgery, via direct connect. The cue for discrimination is a difference in spectral content between the two phonemes. Hence, if certain contrasts cannot be discriminated, this reflects a failure of the cochlea to convey the spectral cue.
Loudness Scaling	Narrowband noise presented at various intensity levels to measure sound comfort at various intensities through the cochlear implant after surgery, via direct connect. This test assesses the identification of sound on a visual analog scale from inaudible to too loud by the recipient.
Pending Outcome Request	Output from the AI system at the end of each session. A list of tests to be completed at the next visit are provided for future optimization of the AI MAP. These may include loudness scaling, audiometry, speech audiometry, and/or phoneme discrimination.
Speech, Spatial, and Qualities of Hearing Scale (SSQ)	A validated metric used as a self-assessment of hearing in everyday life across three hearing domains: speech hearing, spatial hearing, and qualities of sound

3.0 Introduction and background

The goal of this study is to evaluate recipient outcomes and clinician and recipient acceptance of a new Artificial Intelligent (AI) technology. The AI system utilizes novel evaluation measures to provide a standardized approach to post-operative programming (also referred to as MAPping). This technique can be utilized as a clinical tool for the audiologist to use in modifying programming parameters for both existing and newly implanted cochlear implant recipients. As mentioned the AI technology is a tool used by an audiologist to provide programming modifications in a more consistent manner.

One of the novel evaluation methods is via psychophysical tests based in auditory hierarchy skills. These include detection, discrimination, identification and comprehension of auditory stimulus. Tests will be presented via direct auditory input to the sound processor. This module allows for test measures to be presented in a calibrated manner outside of the soundfield through the commercially available wired and wireless programming pods. There are several configurations which can be utilized based on clinician and patient preference as well as the sound processor type. One of these configurations is via the commercially available CP910 sound processor, Personal Audio Cable, and standard of care Cochlear Nucleus Programming Pod as shown in Figure 1 below. The software test module may allow for improved clinician and recipient experience by allowing the aforementioned testing to be delivered directly to the recipient's sound processor outside of a soundfield for both newly implanted and existing cochlear implant recipients.

Additionally, the AI will provide fitting recommendations based on the psychophysical test measures listed above and program parameters which will assist the audiologist during cochlear implant programming sessions. The recommendations by the AI agent is outcome driven based on data from psychoacoustic tests (Bermejo et al, 2013, Varenberg et al 2011, Govaerts et al 2010). In current clinical practice patient programs (also referred to as MAPs) are often modified based on subjective patient feedback. Programming parameter modifications are made in Custom Sound, for Cochlear Nucleus recipients. The program adjustments can vary based on clinical center and audiologist, which may impact patient outcomes in some cases. The AI system provides several advices to potentially improve outcomes, based on data across major cochlear implant systems and individual psychoacoustic data. These Intelligent Agent recommendations can substantially reduce programming time, as it may assist the audiologist in implementing test results to modify the recipient's program (also referred to as a MAP), Figure 2

Figure 1. Personal Audio Cable connection

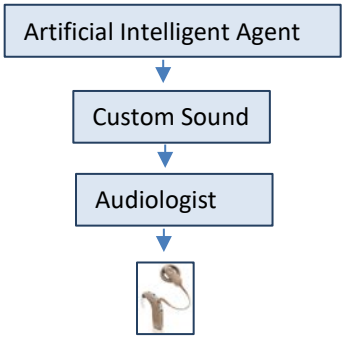


Figure 2. AI system interaction

3.1 Study Objective

Group 1 (Newly Implanted): To compare preoperative speech recognition with an appropriately fit hearing aid to Cochlear Implant (CI) performance at 6 months post-activation using a CNC Monosyllabic Word Test administered in soundfield at 60dBA for the implanted ear.

Group 2 (Existing subjects): To compare performance in subjects using an expert clinician (EC) MAP versus an Artificial Intelligence (AI) MAP on a CNC Monosyllabic Word score administered in soundfield at 60dBA.

4.0 Criteria for Subject Selection

Cochlear Americas expects to enroll a minimum of 30 subjects for Group 1; and a minimum of 50 subjects in Group 2, for Group 2 at up to 8 North American cochlear implant centers. The duration of the multisite study is expected to be up to 2 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 population of those with hearing loss, with no pre-selection based on age (other than being 12 years-of-age or older), ethnicity or gender. To be included in the study, subjects must meet the criteria below. Group 1 (Newly implanted subjects) will participate in the study for 6 months post-activation. Group 2 (Existing subjects) will participate in the study for up to 8 weeks after enrollment. Bilateral cochlear implant recipients may be included in the study, however only one ear will be evaluated.

4.1.1 Inclusion Criteria

- Newly implanted and existing recipient Groups (Groups 1 and 2):
    - Age 12 and older
    - For Group 1 only: CNC word recognition score administered at 60dBA (2 lists) with an appropriately fit hearing aid in the ear to be implanted who are receiving a cochlear implant as standard of care
    - For Group 2 only: 3 months or greater combined experience with Nucleus 5, 6, Kanso, or 7 series sound processor
    - Fluent spoken English skills

4.1.2 Exclusion Criteria:

- Newly implanted and Existing Recipient Groups (Groups 1 and 2):
    - Unrealistic expectations on the part of the subject regarding the possible benefits, risks, and limitations
    - Additional cognitive, medical or social handicaps that would prevent completion of all study requirements
    - Unwillingness or inability of the subject to comply with all investigational requirements
    - Use of an acoustic component in the implanted ear
    - Less than 18 active electrodes
    - Hybrid L Cochlear Implant

NOTE: Bilateral cochlear implant recipients may be enrolled into the study at the Investigational team's discretion. The implanted ear with the poorer performance on CNC words will be enrolled for data collection.

5.0 Methods and Procedures

5.1 Device description

Cochlear implant sound processors to be used in this study may include commercially available Nucleus 5, Nucleus 6, Kanso, or Nucleus 7 series processors. The subject's respective sound processor will be programmed for take home use with the AI MAP or AI AutoMAP only. Expert clinician MAPs should not be loaded to the sound processor for take home use.

5.2 Programming Software Description

Programming of the sound processor is achieved via the commercially available and FDA approved Cochlear Nucleus Custom Sound (CS) software. In addition, the psychoacoustic tests will be used to assess performance of the subject and provide the audiologist with programming parameter suggestions. Each clinical site will be provided a laptop to complete psychoacoustic testing, in addition to CS for use in the study.

5.3 Description of Test Measures

5.3.1 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 speech perception performance of individuals 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 60dBA in the soundfield 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.

5.3.2 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 0º azimuth at +10dB SNR.

5.3.3 Psychoacoustic test battery

This term is an overarching name for the following tests: Speech audiometry, phoneme discrimination, loudness scaling, and audiometry. All tests are completed via Direct Connect and collect data regarding detection, discrimination and identification of sound through the cochlear implant. Results from these tests are incorporated into recommendations for the AI MAP. Specific tests within the psychoacoustic test battery to be completed at each study visit are based on recommendations through the AI software

5.3.3.1 Speech audiometry

For this study, 25 CNC words randomly selected from each list will be administered in quiet at each level equal to 40, 55, 70 and 85dB SPL for speech audiometry. Testing will be completed via Direct Connect and scored as the percentage of correctly repeated phonemes. An average phoneme score will be calculated within the test module, across the four presentation levels.

5.3.3.2 Phoneme discrimination

The phoneme discrimination test is performed using up to 20 pre-defined speech sound contrasting pairs (a-r, u-ʃ, u-a, u-i, i-a, o-a, i-e, m-z, s-ʃ, e-a, u-o, ə-a, ə-o, ə-e, ə-i, z-s, v-z, ə-u, u-y, y-i). Phoneme pairs have been established as linguistically representative and are tested at 70 dB HL in an oddity paradigm (Govaerts et al., 2006). Subjects will be tested via Direct Connect and provide a behavioral response (e.g., hand raise or verbal response) if a discrimination is recorded for the phoneme contrast. Two correct responses are required to be considered as correct identification as scored by the Investigator. Training for at least one phoneme pair will be completed for each study visit to ensure familiarity with the test.

5.3.3.3 Loudness scaling

Loudness scaling testing is completed by presentation of one-third octave narrow band noises centered at 250, 1000, and 4000 Hz. A 1876 ms duration stimulus will be presented randomly twice at 5dB increments between 30 and 80dB HL. Loudness will be scored on a visual analogue scale ranging from 0 (inaudible) to 6 (too loud) by the subject and stimulus will be delivered via Direct Connect. (Varenburg et al. 2011, Govaerts et. al, 2006, Hereeen et al., 2012).

5.3.3.4 Audiometry

Aided audiometric thresholds via direct connect will be obtained using narrow band noise and the standard audiometric technique (as defined in Appendix A) at the following frequencies 125, 250, 500, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz.

5.3.4 Clinician survey

Clinician surveys will be collected, and may be combined with the Site Initiation Visit. These surveys will provide feedback on current clinical models and practices that are clinic centric and variable. Additional survey data regarding experience with newly implanted and existing subjects will be conducted after experience with at least 5 subjects. The surveys after subjects experience will focus on overall audiologist experience. The information gathered will provide data regarding clinician perceived acceptance and information learned with use of the AI system.

5.3.5 Participant Questionnaire

The Speech, Spatial and Qualities of Hearing (SSQ) (Gatehouse & Noble, 2004) is a subject self-assessment in three categories (speech hearing rating scale, spatial rating scale, and sound qualities rating scale). The SSQ is considered a closed-ended and validated self-report assessment of outcome.

5.3.6 Unscheduled Visit

If a subject requires an interim clinical visit for programming, an Unscheduled Visit Form will be completed. Information collected will include reason for visit, activities completed and visit date. Patients may be seen clinically for accessory and device counseling without completion of the Unscheduled Visit Form, however any change in program or MAP settings during these visits will need to be captured.

5.4 Summary of Data Collection Visits

5.4.1 Group 1 Pre-operative testing

- Administer two CNC word lists in the ear to be implanted
- Complete SSQ Questionnaire

5.4.2 Group 1 Visit A:

- Creation of AutoMAPs and takehome MAP with AI
- Clinical counseling
- Send anonymous CDX file to Cochlear

5.4.3 Group 1 Visit B: (3 weeks post Visit A +/- 3 weeks)

- Administer psychoacoustic tests:
- Audiogram→ FOX Initial Advice
- Phoneme discrimination → FOX Standard Advice
- Program with AI MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear

NOTE: Intent is for subjects to have reached at least Gold 3

5.4.4 Group 1 Visit C: (3 months post Visit A +/- 3 weeks)

- CNC Word Test – Two lists at 60 dB(A) in soundfield with AI MAP*

- Implanted ear, contralateral ear plugged
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in soundfield with current MAP*
  Unilateral Aided, ear to be implanted with contralateral ear plugged
- Administer psychoacoustic tests to include at least:
  - Speech audiometry→ FOX Standard Advice
  - Loudness scaling
  - Other pending outcome requests from AI (if any)**
- Program with AI MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear

*NOTE: Soundfield speech perception testing will be completed with patient's preferred processor and program settings

5.4.5 Group 1 Visit D: (6 months from Visit A +/- 3 weeks)

- CNC Word Test – Two lists at 60 dB(A) in soundfield with current MAP*
  - Implanted ear, contralateral ear plugged
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in soundfield with current MAP*
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
- Administer psychoacoustic tests to include at least:
  - Speech audiometry → FOX Standard advice
  - Loudness scaling
  - Other pending outcome requests from AI (if any)
- Program with AI MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear
- Complete SSQ Questionnaire

*NOTE: Soundfield speech perception testing will be completed with patient's preferred processor and program settings

**NOTE: Only complete Pending Outcome Requests (POR) if MAP used for testing at day of visit has POR. Do not complete POR if MAP is not used for day of testing

5.4.6 Group 2 Visit A

- CNC Word Test – Two lists at 60 dB(A) in soundfield with current MAP*
  - Implanted ear, contralateral ear plugged
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in soundfield with current MAP*
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
- Administer psychoacoustic evaluation measures including:
  - Audiometry
  - Phoneme discrimination
  - Loudness scaling
  - Speech audiometry

- Create AI AutoMAP
- Administer psychoacoustic evaluation measures including:
  - Audiometry→ FOX Initial Advice

- Phoneme discrimination→ FOX Standard Advice
- Create AI take home MAP
- Clinical counseling
- Send anonymous CDX file to Cochlear

*NOTE: Soundfield speech perception testing will be completed with patient's preferred processor and program settings

5.4.7 Group 2 Visit B (1 month from Visit A +/- 2 weeks)

- CNC Word Test – Two lists at 60 dB(A) in soundfield with AI MAP from Visit A*
  - Implanted ear, contralateral ear plugged
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in soundfield AI MAP from Visit A*
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
- Administer psychoacoustic tests via direct connect to include:
  - Speech audiometry→ FOX Standard Advice
  - Loudness scaling
  - Other pending outcome requests from AI**
- CNC Word Test – Two lists at 60 dB(A) in soundfield (acute testing of optimized AI MAP)*
  - Implanted ear, contralateral ear plugged
- AzBio Sentences in Noise – One list at 65dB(A) with a +10 dB SNR in soundfield (acute testing of optimized AI MAP)
  - Unilateral Aided, ear to be implanted with contralateral ear plugged
- Subject questionnaire
- Clinical counseling
- Send anonymous CDX file to Cochlear

*NOTE: Soundfield speech perception testing will be completed with patient's preferred processor and program settings
**NOTE: Only complete Pending Outcome Requests (POR) if MAP used for testing at day of visit has POR. Do not complete POR if MAP is not used for day of testing

5.5 Data Analyses

5.5.1 Study Population

Statistical Analysis for this study is addressed in detail in the document entitled "Statistical Analysis Plan for the Clinical Investigation of New CI Delivery Models in a Nucleus CI Population study".

5.5.2 Sample Size

The study is intended to evaluate clinical outcomes and provide clinical guidance in addition to regional experience on the fitting and use associated with AI system. Subject enrollment is estimated to take up to 12 months to recruit subjects across clinical sites. The enrollment period may be extended if required. Statistical Analysis for this study is addressed in detail in the document entitled "Statistical Analysis Plan for the Clinical Investigation of New CI Delivery Models in a Nucleus CI Population study". For Group 1, analysis will be based on a paired t-test. A planned evaluable sample size of 30 subjects with at least 80% power will be provided for a mean difference between preoperative and 6 month performance. For Group 2, analysis will be based on a paired

t-test for non-inferiority. A planned evaluable sample size of 50 subjects with approximately 90% power will be provided with no assumed mean difference between AI MAP and EC MAP, and a non-inferiority margin of 10%.

5.5.3 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).

5.5.4 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.

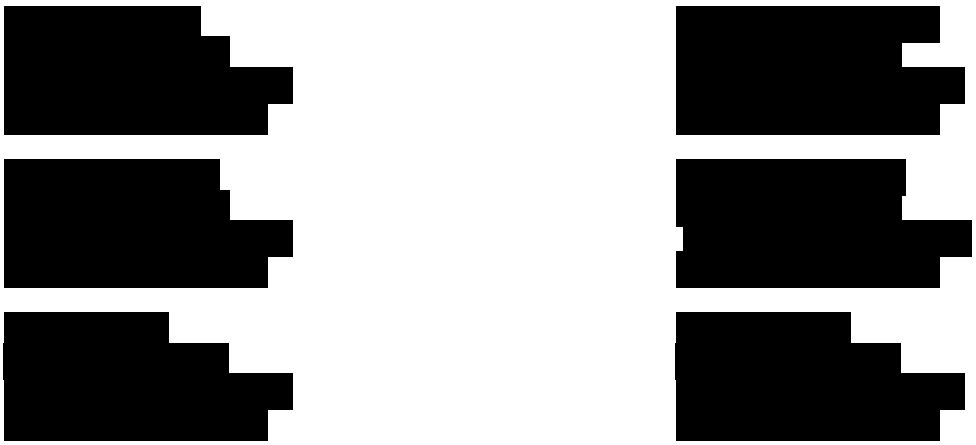
5.5.5 Additional Statistical Analyses

Statistical Analysis for this study is addressed in detail in the document entitled “Statistical Analysis Plan for the Clinical Investigation of New CI Delivery Models in a Nucleus CI Population study”.

5.5.6 Access to Study Documents and Data Monitoring

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

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:



All data generated during this study and the source documents from which they originated are open to inspection by the Sponsor or its representative, 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. Data collection is performed using electronic data capture (EDC) on electronic Case Report Forms

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

5.6 Data Storage and Confidentiality

5.6.1 Confidentiality

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

Copies of the completed CRFs are to be provided to the Sponsor as soon as practical after completion and review. The original CRFs are to be retained by the Investigator for a period of time as determined by local regulations.

5.6.2 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-ART-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,
- ART = an abbreviation for the study, in this case "ART" for the Artificial Intelligent system,
- 0000 = a unique, numeric study site identification.

5.6.3 Release of Medical Information

Subjects will be required to release the exchange of medical information between the Investigator(s) and the Sponsor. This requirement will be clearly identified in the Informed Consent form.

5.1 Transition from Research Participation

5.1.1 Completed Subjects

Subjects in Group 1 will be deemed completed after approximately 6 months post-activation, including completion of evaluation materials (See Section 3.3). Subjects in Group 2 will be deemed completed after approximately eight weeks, including completion of evaluation materials (See Section 3.3). Subjects will continue to receive standard clinical follow-up care at their cochlear implant facility after the study.

6.0 Risk Benefit Statement

It is possible but not guaranteed that advances to cochlear implant technology will improve performance via artificial intelligence programming and clinic models for future recipients. This clinical investigation will help to inform the future development of associated clinical guidance when fitting cochlear implant patients.

6.1 Risk Category

As determined by the Sponsor, this study has been designated as non-significant risk. The cochlear implant, sound processor and physical programming equipment used in this study is standard of care and commercially available.

6.2 Potential Risk and Protection Against Risks

Subjects may experience sounds during mapping that are uncomfortably loud. Mitigation of the risk listed above is similar to that used during clinical cochlear implant mapping wherein the sound processor is removed from the subjects head and/or the stimulation to the sound processor is ceased in Custom Sound. Risks to newly implanted subjects is consistent with commercially cochlear implantation. Risks of cochlear implantation will be detailed in the informed consent.

6.3 Potential Benefits to Subjects

Potential benefits to subjects may include improved outcomes on speech perception outcomes due to programming technology and reduced clinical visits with the modified clinic model schedule while in this study. It cannot be promised that subjects will receive any medical benefits from being in this study.

6.4 Alternatives to Participation

In lieu of study participation, patients may elect to continue standard clinical care for hearing aids if they do not pursue cochlear implantation, or pursue cochlear implantation without study participation. If patients receive a cochlear implant outside this study, programming will not be completed with the programming technologies or modified clinic model used in this study. Patients who have been implanted prior to invitation to participate in the study may be seen for post-operative management of per standard clinical care at their respective institution.

7.0 Subject identification, Recruitment, and Consent/Assent

7.1 Method of Subject Identification and Recruitment

Subjects will be recruited into the study sequentially to ensure a subject pool representative of the general population of those with hearing loss, with no pre-selection based on age (other than being 12 years-of-age or older), ethnicity or gender as described in Section 2.0. The identification and recruitment of subjects will protect patient privacy and be free of undue influence.

7.2 Process of Consent

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 reviewing Institutional Review Board (IRB). An interview (as part of the informed consent process) will be conducted by the surgeon and/or audiologist to inform the subject about rationale for and the details, aims, objectives of the study, study expectations, evaluation schedule, and the risks and benefits of the trial treatment (and alternative treatments), and the extent of the patient's involvement. Written informed consent shall be obtained from each subject after this explanation. After reviewing the Informed Consent Form, the subject 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 subject 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 subject twill then be given a copy of the signed Informed Consent Form to take home. The informed consent process is intended to be completed after standard of care surgery for Group 1 subjects, but may be completed pre-operatively if deemed appropriate by the Investigator.

The Investigator is responsible for ensuring that all patients give written informed consent prior to any study-related examination or activity. All patients shall sign and date the Informed Consent Form, and a copy of the Informed Consent Form shall be given to the patient. The Sponsor and the Investigator(s) shall avoid improper influence on or inducement of the subject, monitor, the Investigator(s) or other parties participating in or contributing to the clinical investigation.

7.3 Subject Capacity

Adult subjects participating in this study will have the capacity to provide informed consent as assessed by the Investigators. The only anticipated exception this is minors, for which assent will be obtained in addition to parental consent.

7.4 Subject/Representative Comprehension

Subject/Representative comprehension for participation in this study will have the capacity to provide informed consent as assessed by the Investigators on behalf of themselves or minor subjects. With regard to minor subjects, assent will be obtained in addition to parental consent.

7.5 Consent Forms

The informed consent form provided for this study will meet requirements for specific sections as described in 21 CRF 50.25.

7.6 Documentation of Consent

A subject is not considered enrolled until a properly executed Informed Consent Form has been obtained and inclusion/exclusion information has been reviewed and approved by Cochlear Americas, as evidenced by the return of a study approval form signed by a Cochlear Americas representative.

7.7 Costs to the Subject

Costs to subjects in this study include billing newly implanted subjects and/or their insurance company for a Nucleus cochlear implant system and for surgery. The insurance company will be billed for any medical, surgical, or audiological treatment which may be needed after receiving the cochlear implant. Cochlear Americas will not for any audiology or medical evaluation conducted before or after surgery. Subjects will not be reimbursed by Cochlear Americas for the surgery, programming of the device, or any therapy received. These services are all standard components of learning to hear with a cochlear implant.

Tests and procedures that are done only for the study will not be billed to the subject's insurance company. It is recommended subject's talk with their insurance company about its payment policy for standard medical care given during a research study. If the subject's insurance company does not pay, they may be billed for those charges. Subjects are responsible for, and will have to pay for, transportation to and from the study visits.

7.8 Payment for Participation

Subjects in Group 1 and Group 2 will be paid $12.50/hour for study visits completed. If a subject withdraws from the study before completing all study visits, they will be compensated $12.50/hour for the study visits which were completed. In order to receive payment for participation, subjects will need to complete a W-9 form, which is required because study payments for time are taxable.

Additionally, subjects in Group 1 will receive a comprehensive warranty on all parts connected with the system for 5 years following the initial activation of the implant. This is in addition to the standard warranty on internal and external equipment provided by Cochlear Americas.

7.9 Institutional Review Board

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

Study procedures will not be changed without mutual agreement between the Sponsor and the Investigator(s). Changes will be implemented in a signed protocol amendment, and for significant changes, approval will be obtained from the IRB.

8.0 Reporting Process for Adverse Events and Device Deficiencies

8.1 Definitions

8.1.1 Adverse Event (AE)

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or procedure.

8.1.2 Adverse device effect (ADE)

An adverse device effect is an adverse event related to the use of an investigational medical device. This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

8.1.3 Device deficiency (DD)

A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labelling. For the purposes of this study, the device of study is the AI software and related functions to complete testing and/or programming.

8.1.4 Serious Adverse Event (SAE)

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

- led to death
- led to serious deterioration in the health of the subject, that either resulted in
- a life-threatening illness or injury, or
- a permanent impairment of a body structure or a body function, or
- in-patient or prolonged hospitalization, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

- led to fetal distress, fetal death or a congenital abnormality or birth defect

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

8.1.5 Serious adverse device effect (SADE)

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

8.1.6 Unanticipated Adverse Device Effects

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

8.2 Assessment and Reporting of Adverse Events and device deficiencies

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

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

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

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

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

8.3 Protocol Deviations

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

9.0 References

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Govaerts PJ, Daemers K, Yperman M, De Beukelaer C, De Saegher G, De Ceulaer G. Auditory speech sounds evaluation (A§E®): a new test to assess detection, discrimination and identification in hearing impairment. Cochlear Implants International 2006; 7(2): 97-106.

Appendix A: Procedural considerations

- Pre-CI (Hearing aid condition) and post-CI (Cochlear Implant condition) testing may be completed in the soundfield 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.

- Additional test set-up post-implantation for Group 1, or for Group 2 includes testing via direct connect, which is described as direct connection to the sound processor via the Personal Audio Cable and Programming Pod. Calibration will be completed prior to initiation of any test and will be calibrated within the test system.

- Speech and hearing evaluations completed in the soundfield will be completed 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).

- Speech and hearing evaluations completed with Direct Connect testing will be completed in a quiet room within the clinical site.

- 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.

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