INVESTIGATIONAL PLAN

Safety and efficacy of remote programming of Nucleus® cochlear implants

Version 1.0

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IDE #

G150238

Study Sponsor:

Cochlear Americas

13059 East Peakview Avenue

Centennial, CO 80111

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 remote programming of Nucleus® cochlear implants."**

Clinical Investigational Site

Primary Investigator's Name (print)

Title

Signature

Sponsor Representative

Title

Signature

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TERMS, DEFINITIONS, AND ABBREVIATIONS

Terms/Abbreviations	Definition
AE	Adverse Event
CI	Cochlear Implant
Charge	Unit of electrical stimulation
Custom Sound™	Clinical programming software for Nucleus cochlear implant systems
Facilitated MAP	A MAP programmed remotely with the assistance of a facilitator
Facilitator	A trained staff member at the programming site
IDE	Investigational Device Exemption
Live Programming	Traditional face to face programming interaction between a recipient and an audiologist at the same physical location
MAP	A program that defines the individualized parameters of recipients for a specific speech coding strategy
Nucleus® 5 Sound Processor	BTE sound processor to be used in the evaluation
Nucleus® 6 Sound Processor (CP910 or CP920)	BTE sound processor to be used in the evaluation
Primary Audiologist	The audiologist who regularly provides programming services to the subject
Remote Programming	A programming interaction between a recipient and an audiologist that occurs via telecommunication technology when the two parties are at different physical locations
Self MAP	A MAP programmed remotely without the assistance of a facilitator

STUDY SUMMARY

Title	Investigation of consistencies and performance of cochlear implant MAPs programmed via telecommunication
Study Sites	Up to 5 North American centers
Study Duration	Up to 12 months
Study Time	3-4 months for each subject
Study Population	Up to 40 subjects aged 12 years or greater
Design Overview	The study will be conducted in a repeated measures design
Primary Objective	To demonstrate the safety and efficacy of CI programming via telecommunication.
Study Intervals	**Visit 1** (at least 1 month but no more than 12 months after a regular programming session) **Visit 2** (within one month after Visit 1) **Visit 3** (2-4 weeks after Visit 2) **Visit 4** (2-4 weeks after Visit 3) **Visit 5** (2-4 weeks after Visit 4)
Primary Safety Endpoint	Characterize the safety profile of device and/or procedure related adverse events associated with facilitated remote MAP programming, unassisted MAP programming and audiologist live MAP programming
Co-Primary Efficacy Endpoints	1. Demonstrate that performance on CNC words using a remotely programmed facilitated MAP is no worse than when using a live programmed MAP 2. Demonstrate that performance on CNC words using an unassisted remotely programmed MAP is no worse than when using a live programmed MAP
Secondary Efficacy Endpoint	Demonstrate non-inferiority of unassisted remote MAP programming compared to facilitated MAP programming via performance on CNC words.

INTRODUCTION

Telemedicine is the practice of using technology to provide remote clinical services over the internet. In that cochlear implantation requires regular programming visits with an audiologist, the use of telemedicine can prove valuable and efficacious for recipients, particularly those who live far from clinics, have limited transportation options, or are medically fragile. Telemedicine can also be utilized for direct high level trouble shooting between recipients, clinicians, specialists, and manufacturers.

Primary medicine and some of its auxiliary services have already entered into the arena of telepractice with successful outcomes (Uscher-Pines, et al., 2014; Darkins, et al., 2013; Mashima & Doarn, 2008). Staying on track with this technological advent, resourceful clinicians and researchers have begun exploring the validity of remote audiological intervention. Documented outcomes suggest comparable results between traditional live programming and remote programming measures (Eikelboom, 2014; McElveen, 2010; Ramos, 2009; Rodriguez, 2014; Samuel, 2014; Wesarg, 2010). Performance validation of remotely programmed maps as examined by Hughes (2012) and Goehring (2012) denotes that any changes in speech perception scores may be a result of sub-optimal testing environments as opposed to programming delivery method. Furthermore, when probed, most study participants reported satisfaction with the remote programming sessions, and indicated they would be interested in utilizing the technology for future appointments.

Some points of interest that have arisen include the capacity to assess physical integrity of devices, detection of adverse events over a telecommunication medium, remote programming in the pediatric population, duration of CI use prior to remote sessions, professional state licensure requirements, and reimbursement. These topics should be considered for future investigation.

Given that telemedicine is being widely utilized, and studies show minimal to no change in aided thresholds and MAP Threshold (T) and Comfort (C) levels, this investigation aims to validate the safety and efficacy of remote cochlear implant programming in an effort to establish clinical support for this practice and subsequently increase access to recipients. Specifically, this study will show that speech recognition scores obtained using remotely programmed MAPs are no worse than those obtained using live programmed MAPs. Additionally, it will demonstrate that live MAPping adverse events are consistent with and not inferior to remote MAPping adverse events. Finally, this study will capture overall electrical charge of remotely programmed MAPs, and explore any inconsistencies between the audiologist-to-facilitator model and the audiologist-to-recipient model of remote service delivery.

STUDY OBJECTIVES

Primary Objectives

The primary objective of this multi-site study is to investigate the safety and efficacy of programming cochlear implants through telecommunication.

Safety will be determined by characterizing the safety profile of device and/or procedure related adverse events associated with facilitated remote MAP programming, unassisted MAP programming and audiologist live MAP programming. An adverse event (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.

Efficacy will be determined by showing that performance on the CNC word recognition test using a remotely programmed MAP is no worse than when using a live programmed MAP.

INVESTIGATIONAL PROTOCOL

Subject Selection

The proposed investigation will take place in the United States. Up to 5 clinical sites and up to 40 subjects will be enrolled. Due to time needed for site training and subject recruitment, the total duration of this multi-site study will be 12 months.

Inclusion Criteria

- Individuals aged greater than 12 years that are native English speakers and are capable of completing the study evaluation as deemed by their primary audiologist
- Unilateral or bilateral cochlear implant recipients of a CI24RE, CI422 or CI500 series implant who are in possession of a backup sound processor
- A minimum of 12 months' experience with a CP800 or CP900 series sound processor, and current MAP programmed within 12 months prior to Visit 1
- Willingness to participate in and to comply with all requirements of the protocol
- Able to demonstrate protocol competence as confirmed by primary audiologist

Criteria for Exclusion

- Unrealistic expectations on the part of the subject, regarding the possible benefits, risks, and limitations of remote service delivery
- Unwillingness or inability of the candidate to comply with all investigational requirements
- Additional handicaps that would prevent or restrict participation in the audiological evaluations

- Inability to demonstrate basic technological skills for simple computer-based tasks and device connecting after training by primary audiologist

Investigational Procedures

Design Overview

Cochlear implant recipients aged greater than 12 years of age will be asked to participate in this clinical study. A single-subject research design (in which each subject serves as his or her own control) is appropriate since it accommodates the heterogeneity that characterizes hearing-impaired populations. Subjects will be tested at three intervals: the first, third, and last of five total visits.

At **Visit One**, the subjects will be screened and consented by their primary audiologist. They will complete speech testing in the unilateral condition, using their current MAP which they must have been using for no more than 12 months. Subjects will schedule Visit 2 to fall within one month after Visit 1.

Visit Two will take place at a pre-determined site, different than the subject's primary programming center. The subjects will participate in a remote location programming session conducted by their primary audiologist via telecommunication, with on-site assistance provided by a trained facilitator. This MAP will be referred to as the Facilitated MAP.

Subjects will return home and use this new program for 2-4 weeks, after which time they will return to their primary programming center for Visit 3.

For **Visit Three** (2-4 weeks after Visit 2), subjects will return to their primary programming center for speech testing using their remotely programmed MAP (Facilitated MAP), and to complete a comparative survey.

Visit Four will occur 2-4 weeks after Visit 3 at the same pre-determined site as Visit 2. The subjects will participate in a second remote programming session conducted by their primary audiologist via telecommunication, but the subject will serve as his or her own facilitator. This MAP will be referred to as the Self MAP.

Subjects will return home and use this new program for 2-4 weeks, after which time they will return to their primary programming center for Visit 5.

At **Visit Five**, subjects will complete speech testing using their second remotely programmed MAP (Self MAP). Subjects will also complete a comparative survey and a questionnaire regarding their experience with remote programming.

The following study procedures will be completed:

MAP Programming Methods

Subjects will be programmed at a remote clinic location by their primary audiologist programming via telecommunication. The subjects' existing "familiar" MAP will remain in slot #1. Audiologists will save each remotely programmed MAP into slot #2, overwriting any previous program in that slot (subjects will be able to have their choice of program re-entered into slot #2 after they have completed participation in this study). Audiologists will anonymize and export the MAP to the sponsor after each programming session.

System Requirements

Each remote site will require a programming computer, a programming pod, and a programming cable. Computers will be outfitted with a password locked Custom Sound application to allow software access to the remote audiologist meanwhile preventing any accidental programming by the recipient. Each site will also need microphone/speaker/camera capabilities on the computer for communication between the audiologist and the subject during the remote sessions. A wired or wireless internet broadcasting system is acceptable with a minimum connection speed of 1 megabit/sec in both directions.

The programmer site will require the same computer, software, and connection specifications as outlined above.

Speech Perception Testing

Speech perception testing will be completed at Visit One, Visit Three, and Visit Five.

Speech perception testing to evaluate the program settings will be assessed in the unilateral condition (cochlear implant ear only) and the contralateral ear will be plugged (or the contralateral CI will be removed if applicable).

Speech perception testing will be completed at the subject's primary clinic site, and evaluation lists will be randomized.

Evaluation Materials and Test Conditions

- At Visit One, Visit Three, and Visit Five, participants will have their speech perception tested using CNC words (Peterson & Lehiste, 1962) in quiet presented at 60 dBA as indicated in Figure 1.
- Each participant will complete 2 full lists (50 words per list) per test condition

For the purpose of evaluating the remotely programmed MAPs, test condition refers to a program slot number:

1. Test condition: Familiar program – Program 1: Participant's current program that he/she was utilizing prior to the remote MAPping (Tested at Visit 1)

2. Test condition: Remote program – Program 2: the Facilitated MAP programmed remotely at Visit 2 (tested at Visit 3) and the Self MAP programmed remotely at Visit 4 (tested at Visit 5).

Figure 1: Test Setup for Speech Recognition Testing

Self-Assessment/Subjective Questionnaires

The following subjective questionnaire will be completed at Visit 2 and Visit 4 after the remote programming session.

Remote Programming Satisfaction Survey
This in-house survey uses a satisfaction rating scale to gather subjects' opinions regarding the ease, quality, and comfort of the remote programming sessions.

The following self-assessment/subjective questionnaires will be completed at Visit 3 and Visit 5, following home use of the remotely programmed MAPs.

The Speech, Spatial and Qualities of Hearing Questionnaire – C (SSQ – C)
The SSQ-C (Gatehouse & Noble, 2004) will be used as a subject self-assessment in three categories (speech hearing rating scale, spatial hearing rating scale, and sound qualities rating scale). The SSQ-C is the "comparative" version of the SSQ. It can be used for comparing two different hearing technologies. In this study, the SSQ-C will compare the subject's familiar map (Program #1) and a remote MAP located in Program slot #2.

The following subjective questionnaire will be completed at the final visit (Visit 5).

Telemedicine Experience Questionnaire
This in-house survey was specifically designed to examine subjects' evaluations of the telemedicine experience. It includes a response rating scale, as well as the opportunity for open ended feedback.

Methods

VISIT 1

Step 1: Subject will arrive at his/her primary programming center. No programming will be completed at this visit.

Step 2: The subject will read and sign the informed consent form.

Step 3: The subject's primary audiologist will orient him/her to the programming equipment, detailing how to hook up the speech processor to the computer, how to launch the necessary applications, and how to utilize the chat function. The subject will demonstrate competency in these steps as deemed appropriate by the audiologist.

Step 4: Speech perception testing will be completed using Program 1 (subject's familiar program).

Step 5: The cdx file for the subject's current MAP will be anonymized and exported to the sponsor.

VISIT 2 (occurring within 1 month after Visit 1)

Step 1: The subject will arrive at the remote location site.

Step 2: This session will be assisted by a trained facilitator. The subject will be programmed by the remotely located primary audiologist. This program will be saved in Program slot #2, and the cdx file will be anonymized and exported to the sponsor.

Step 3: The subject will complete the Remote Programming Satisfaction Survey.

Step 4: The subject will use this Facilitated MAP at home for 2-4 weeks.

VISIT 3 (2-4 weeks after Visit 2)

Step 1: The subject will return to his/her primary programming center.

Step 2: Speech perception testing will be completed using the Facilitated MAP (Program 2).

Step 3: The Subject will complete the SSQ-C comparing the familiar MAP and the Facilitated MAP.

VISIT 4 (2-4 weeks after Visit 3)

Step 1: The subject will arrive at the remote location site.

Step 2: This session will be conducted with the subject acting and his/her own facilitator. The subject will be programmed by the remotely located audiologist. This

program will be saved in Program slot #2 (taking the place of the previous MAP in that slot), and the cdx file will be anonymized and exported to the sponsor.

Step 3: The subject will complete the Remote Programming Satisfaction Survey.

Step 4: The subject will use this Self MAP at home for 2-4 weeks.

VISIT 5 (2-4 weeks after Visit 4)

Step 1: The subject will return to his/her primary programming center.

Step 2: Speech perception testing will be completed using the Self MAP (Program 2).

Step 3: The subject will complete the SSQ-C (comparing the familiar MAP and the Self MAP), and the Telemedicine Experience Questionnaire.

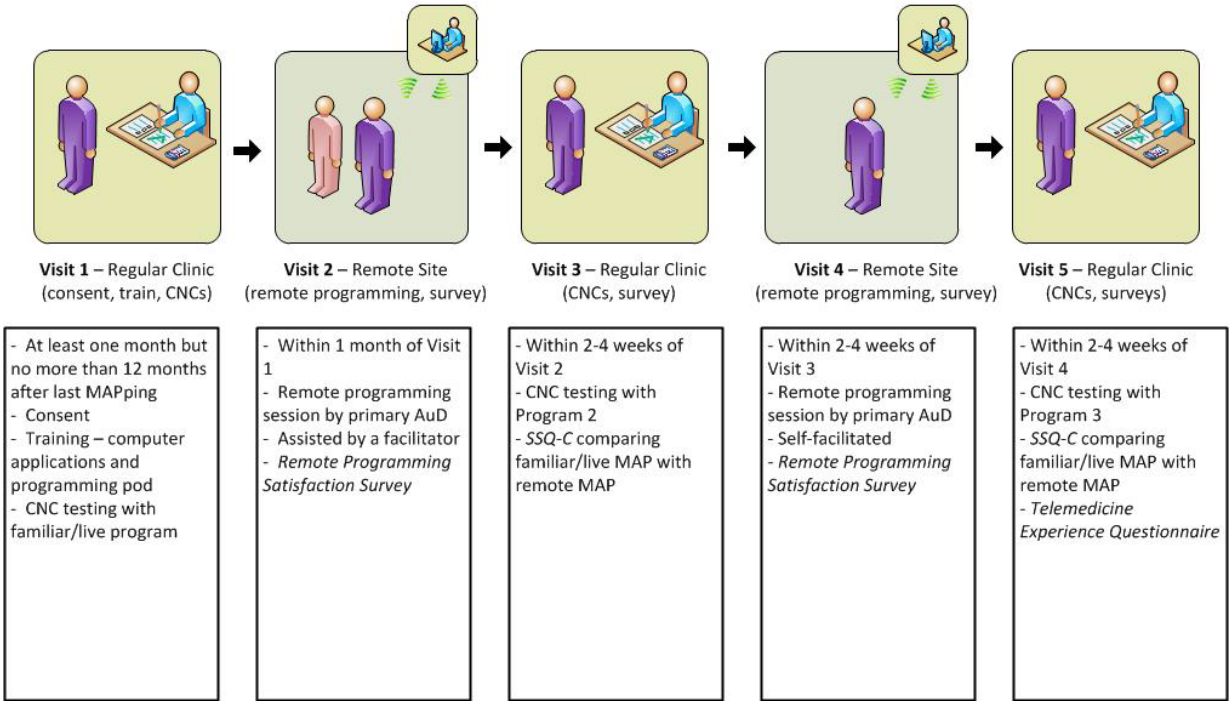

Figure 2: Study visit flow chart

Endpoint Testing

Primary Safety Endpoint: ***Characterize the safety profile of device and/or procedure related adverse events associated with facilitated remote MAP programming, unassisted MAP programming and audiologist live MAP programming***

Safety Endpoint testing will occur at Visit 2 and Visit 4.

- Recipients will be MAPped via telecommunication by a remotely located audiologist.
- Any adverse events associated with the MAPping will be recorded on the New Adverse Event Reporting Form. Any AEs identified at Visit 2 or Visit 4 will be re-evaluated at subsequent visits and updated on the Follow Up Adverse Event Reporting Form.

Co-Primary Efficacy Endpoint 1: ***Demonstrate that performance on CNC words using a remotely programmed facilitated MAP is no worse than when using a live programmed MAP***

Efficacy Endpoint 1 testing will occur at Visit 1 and Visit 3.

- **Visit 1:** Speech perception scores will be obtained in Program 1 (familiar/Live)
- **Visit 3:** Speech perception scores will be obtained in Program 2 (Facilitated MAP)

Co-Primary Efficacy Endpoint 2: ***Demonstrate that performance on CNC words using an unassisted remotely programmed MAP is no worse than when using a live programmed MAP***

Efficacy Endpoint 2 testing will occur at Visit 1 and Visit 5.

- **Visit 1:** Speech perception scores will be obtained in Program 1 (familiar/Live)
- **Visit 5:** Speech perception scores will be obtained in Program 2 (Self MAP)

Secondary Efficacy Endpoint: ***Demonstrate non-inferiority of unassisted remote MAP programming compared to facilitated MAP programming via performance on CNC words.***

Efficacy Endpoint 2 testing will occur at Visit 3 and Visit 5.

- **Visit 3:** Speech perception scores will be obtained in Program 2 (Facilitated MAP)
- **Visit 5:** Speech perception scores will be obtained in Program 2 (Self MAP)

Test Materials:

- CNC word list presented at 60 dBA (subject facing speaker) with contralateral ear plugged. Two lists (of 50 words each) will be completed for each condition. Score each test condition for % of words correct.

Note: The test material lists will be randomized.

Table 1: Summary of data collection visits

Test Material and Condition	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
CNC words in Program 1 (original/Live program)	X				
CNC words in Program 2 (remote program)			X		X
Remote Programming Satisfaction Survey		X		X	
SSQ-C			X		X
Telemedicine Experience Questionnaire					X

MAP Analysis:

Anonymized Live MAP, Remote Facilitated MAP, and Remote Self MAP cdx files will be submitted by the audiologist to the sponsor for analysis of electrical charge data.

ADVERSE DEVICE EFFECTS

To monitor subject safety throughout this IDE study, any procedure or device related adverse events will be recorded. Information on all adverse events will be maintained by event type. The investigator will complete an Adverse Event form if any adverse event is reported or observed for a subject during this IDE, even if they were acknowledged as risk factors in the Informed Consent form.

Adverse device effects refer to any undesirable clinical or medical occurrence associated with use of the device or participation in the study. Any/all adverse device effects are to be recorded via the Adverse Event form. Adverse device effects will be reported if observed, even if they were acknowledged as risk factors in the Informed Consent form.

UNANTICIPATED ADVERSE DEVICE EFFECTS

Unanticipated adverse device effects refer to any event not identified above 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)]

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

DATA ANALYSES

Sample Size

Based on the variability observed in earlier studies, it was determined using PASS (NCSS Statistical Software) that a minimum of 26 subjects would provide at least 90% power for hypothesis testing of the two co-primary endpoints at the 0.025 alpha level.
The planned sample size of 40 subjects will provide adequate power for hypothesis testing of the two coprimary endpoints at the 0.025 alpha level. The following general assumptions have been made:

- T-tests of difference scores to test for non-inferiority with a non-inferiority margin of 10% for CNC word recognition
- One-sided 0.025 alpha level
- Assumed distribution for population (standard deviation)
- Desire for 90% power

The power analyses for the primary test metrics are provided below.

Table 2: Sample size calculation for CNC word recognition

Scenario (Non-inferiority)	Minimum Evaluable Sample Size Required
One-sided 0.025 alpha, 90% power, SD = 15%, NIM = 10%, true difference = 0	26

Additional Statistical Analyses

Statistical Analysis for this study is addressed in detail in the document entitled “Statistical Analysis Plan: Use of telemedicine in the remote programming of Nucleus® cochlear implants.”

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 Investigators or their designee and reviewed by the Sponsor.

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