Clinical Investigation Plan

Investigation Title: A prospective, single centre, single-blinded, within-subject investigation, on the effect of stimulation parameter changes, and monopolar and dual-electrode mode changes, on speech perception in experienced adult cochlear implant recipients.

Short Title:	**DUAL study**
CIP Number:	**CLTD5853**
Version and Date:	**Refer to system version control**
Sponsor:	**Cochlear Limited** **1 University Avenue,** **Macquarie University** **NSW 2109** **Phone: 02 9428 6555**

NCT06298396

This clinical investigation shall be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, International Standard ISO 14155:2020 Clinical investigation of medical devices for human subjects - Good Clinical Practice, and any regional or national regulations, as applicable.

Manufacturer	Cochlear Limited 1 University Avenue, Macquarie University NSW 2109 Phone: 02 9428 6555
Sponsor Organisation	Cochlear Limited 1 University Avenue, Macquarie University NSW 2109 Phone: 02 9428 6555
Funding Source	Sponsoring Organisation
Principal Investigator	[redacted]
Clinical Research Organisation	Avania Pty Limited 13/76 Reserve Road Artarmon, NSW 2064
Contract Services	N/a
Safety Contact	CLTD-SafetyMonitor@cochlear.com

INVESTIGATOR AGREEMENT

Principal Investigator Approval and Declaration

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

I also confirm that I will strictly adhere to the requirements therein and undertake to ensure that all staff with delegated responsibilities in the conduct of this CIP have read, understood and will strictly adhere to the requirements therein. This CIP will not be implemented without prior written approval from the Ethics Committee, any applicable National Competent Authorities, and the Sponsor. If amendments to this plan become necessary, written approval by the Ethics Committee and any applicable National Competent Authorities will be obtained before the changes are clinically implemented per the amendment, except under emergency circumstances to protect the rights, safety, and well-being of subjects.

I also agree that my personal information may be provided to regulatory agencies and public clinical trial registry platforms, and stored in their systems in order to comply with regulatory requirements. Examples of the type of personal information include my name, signature and summary of qualifications.

Name	**Title**
	Principal Investigator
Signature	**Date**

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1 DEFINITIONS AND ABBREVIATIONS

Table 1: List of abbreviations

Term	Description
ACE	Advanced Combination Encoder
ADE	Adverse Device Effect
AE	Adverse Event
AESI	Adverse event of special interest
ARTG	Australian Register of Therapeutic Goods
BKB sentences	Bamford-Kowal-Bench sentences
CDI Tool	Cochlear Device Interface Tool
CI	Cochlear Implant
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CL	Current level
CNC	Consonant Nucleus Consonant
CRF	Case Report Form
CRO	Contract Research Organisation
CTN	Clinical Trial Notification
dB	Decibel
DCF	Data Clarification Form
DD	Device Deficiency
EC	Ethics Committee Synonymous abbreviations/terms include: IRB (Institutional Review Board) IEC (Institutional Ethics Committee or Independent Ethics Committee) HREC (Human Research Ethics Committee)
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EOS	End of study
FF	Forward Focus
GCP	Good Clinical Practices
IB	Investigator's Brochure
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors

Term	Description
IDMC	Independent Data Monitoring Committee
IFU	Information for use
IMD	Investigational Medical Device
IPG	Inter phase gap
ITT	Intent-To-Treat
LP1	Low-power 1 MAP uses wider PW (50µs) & IPG (12µs)
LP2	Low-power 2 MAP uses wider PW (100µs) & IPG (28µs) and lower rate (500Hz)
LP3	Low-power 3 MAP uses wider PW (100µs) & IPG (28µs), lower rate (500Hz) and dual-electrode mode
NA	Not applicable
NCA	National Competent Authority
PI	Principal Investigator
PIL	Principal Investigator List
PMS	Post-Market Surveillance
PP	Per Protocol
PW	Pulse width
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Switching acceptability rating
SD	Standard deviation
SNR	Signal to noise ratio
SOP	Standard Operating Procedure
SPL	Sound pressure level
SRT	Speech reception threshold
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A prospective, single centre, single-blinded, within-subject investigation, on the effect of stimulation parameter changes, and monopolar and dual-electrode mode changes, on speech perception in experienced adult cochlear implant recipients.
Short title	DUAL
Investigation number	CLTD5853
Name of investigational medical device(s)	The IMD for this investigation is dual-electrode mode configuration of stimulation mode in the firmware of the Nucleus 7 (CP1000), Nucleus 8 (CP1110) and Kanso 2 (CP1150) sound processors outside of the functionality of the commercial system. [redacted]
Intended use of investigational medical device(s)	Regulatory status of IMD: Sound processor Post-market; Non-exposed fitting parameter (stimulation mode) in software: Pre-market The IMD for this investigation is dual-electrode mode configuration of stimulation mode in the firmware of the CP1000, CP1110 and CP1150 sound processors outside of the functionality of the commercial system. The CP1000, CP1110 and CP1150 sound processors and its firmware has been approved in Australia under ARTG. The sound processors are intended to be used with a Nucleus Cochlear implant which is intended for restoration of hearing sensation by electrical stimulation of the auditory nerve in patients with moderately severe to profound sensorineural hearing loss. The intended use of the dual-electrode stimulation mode falls within the approved intended purpose description. CDI Tool is a research only software used to program the investigational devices. As this software in not approved in Australia under ARTG, this study will be conducted under the Clinical Trial Notification (CTN) scheme.
Name and description of comparator device/product(s)	Program using the default set of electrical stimulation parameters created with Custom Sound software.
Estimated recruitment period	7 months
Expected duration per subject	2 months
Number of subjects planned	20
Number of investigational sites planned	1
Inclusion criteria	1) Implanted with the CI600 Series (CI612, CI632, CI622, CI624), CI500 Series (CI512, CI513, CI532, CI522) or Freedom Series (CI24RE(CA), CI24RE(ST), CI24RE(CS), CI422) 2) At least three months after activation of the cochlear implant. 3) Eighteen years or older at the time of consent. 4) User of 900Hz ACE (Advanced Combination Encoder) strategy MAP.

	5) Score of 20% or more for CNC words presented at 60dBSPL with CI alone in the test ear. 6) Fluent speaker in English. 7) Willing and able to provide written informed consent.
Exclusion criteria	1) One or more electrodes turned off in the MAP used regularly. 2) Unable or unwilling to comply with the requirements of the clinical investigation as determined by the investigator. 3) Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child or sibling. 4) Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of the investigation. 5) Current participation, or participation in another interventional clinical study/trial in the past 30 days, involving an investigational drug or device (unless the other investigation was/is a Cochlear sponsored investigation and determined by the investigator or Sponsor to not impact this investigation).

Objectives and Endpoints	
Primary Objectives	**Primary Endpoints**
1) To evaluate speech perception in quiet with default and LP1[1] MAPs	1) Paired difference in percentage CNC Words correct between default and LP1 MAPs in quiet setting
2) To evaluate speech perception in noise with default and LP1 MAPs	2) Paired difference in dB SRT (AuSTIN) between default and LP1 MAPs in noise
Secondary Objectives	**Secondary Endpoints**
1) To evaluate speech perception in quiet with LP1 and LP2[2] MAPs	1) Paired difference in percentage CNC Words correct between LP1 MAP and LP2 MAP in quiet setting
2) To evaluate speech perception in noise with LP1 and LP2 MAPs	2) Paired difference in dB SRT (AuSTIN) between LP1 and LP2 MAPs in noise
3) To evaluate speech perception in quiet with LP1 and LP3[3] MAPs	3) Paired difference in percentage CNC Words correct between LP1 and LP3 MAPs in quiet setting
4) To evaluate speech perception in noise with LP1 and LP3 MAPs	4) Paired difference in dB SRT (AuSTIN) between LP1 and LP3 MAPs in noise
5) To evaluate acceptance of switching between LP2 and LP3 MAPs	5) Ratings on switching acceptability rating
Exploratory Objectives	**Exploratory Endpoints**
1) To evaluate speech perception in quiet with LP2 and LP3 MAPs	1) Paired difference in percentage CNC Words correct with LP2 and LP3 MAPs in quiet setting
2) To evaluate speech perception in noise with LP2 and LP3 MAPs	2) Paired difference in dB SRT (AuSTIN) between LP2 and L3 MAPs in noise setting

[1] [redacted]

3) To evaluate adult cochlear implant subjective hearing performance and sound quality with LP1 and LP3 MAPs	3) Paired difference in global SSQ12 scores after experience with LP1 and LP3 MAPs

3 SCHEDULE OF EVENTS

Visit Type	Screening	Visit 1[b]	Visit 2	Visit 3	Additional visits[c]	EOS[d]
Timing of Investigation		**Day 0**	**Week 4**	**Week 8**	**NA**	**NA**
Visit window (±)	NA	**NA**	**Min 4 weeks**	**Min 4 weeks**	**NA**	**NA**
Procedures						
Written informed consent	X					
Demographics	X					
Eligibility	X					
Hearing history	X					
Device history	X					
Medical history	X					
Mapping		X				
Speech perception testing – Words in Quiet (CNC words at 60dB)	X[a]		X	X	X[c]	
Speech perception testing – Sentences in Noise (AuSTIN sentences)			X	X	X[c]	
Switching acceptability rating (SAR)			X	X	X[c]	
SSQ12 Questionnaire			X	X	X[c]	

Clinician log		X				
Concomitant medications/therapies	X	X	X	X	X	X
Adverse Events		X	X	X	X	X
Device Deficiencies		X	X	X	X	X
Device exposure		X	X	X	X	X

[a] To be completed if historical records for CNC words (60dB) is not available to assess eligibility

[b] Visit 1 can be conducted on the same day as screening

[c] Optional; to be conducted if predefined visit procedures could not be completed for any reason

[d] End of study (EOS) may be conducted on same day as visit 3 or on an additional visit.

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

Mapping is an essential part of programming Nucleus cochlear implants (CIs) to provide electrical stimulation to the auditory system, which is perceived within the brain as sound. Generally, a program or "MAP" is created for the CI patient by setting threshold levels (T-levels; the minimal amount of electrical stimulation required for the auditory system to perceive sound) and comfort levels (C-levels; the upper limit of electrical stimulation judged to be most comfortable, or loud but comfortable). This process is typically done approximately 2-4 weeks post-implantation and is repeated at regularly scheduled intervals throughout the patient's lifetime to ensure maximum benefit. To ensure effective stimulation with a CI, the MAP levels need to be set below the voltage compliance limits of the system. Several parameters listed below can affect the ability to set levels within compliance limits. CI recipients use their sound processors all day, every day. Therefore, it is important to ensure that the battery life is as long as possible. Some of the MAP parameters listed below may also influence battery life.

Pulse width (PW): In Nucleus CIs, a biphasic pulse is used to stimulate the auditory nerve fibers in the cochlea. PW refers to the duration of each phase of the biphasic pulse used for stimulation and is expressed in microseconds (µs). Figure 1 shows a schematic illustrating PW. A low PW of 25 or 37µs is used by default for creating MAPs with Nucleus CI to allow for high stimulation rates. Increasing the PW helps reduce the T and C levels, ensuring that the MAP levels are within compliance limits. Wider PW is also useful in reducing non-auditory sensations such as facial nerve stimulation. The Custom Sound 5.2 software and newer versions have an “Auto Pulse Width” feature that automatically widens the PW on all channels to bring them back into compliance.

Inter-phase gap (IPG): The IPG refers to the duration of the interval between the two phases of a biphasic electrical pulse used for stimulation. Figure 1 shows a schematic illustrating IPG. T and C levels reduce when IPG is increased, and this may help ensure that the MAP levels are within compliance limits. One of the strategies to reduce non-auditory sensations such as facial nerve stimulation is to increase the IPG.

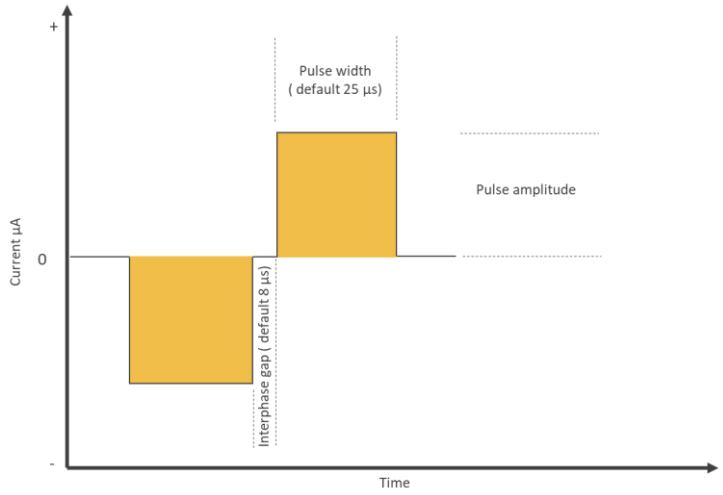

Figure 1: Schematic illustrating pulse width and interphase gap

Stimulation rate: The stimulation rate refers to the frequency (in Hz) of the biphasic current pulse delivered to a channel in a CI. In Nucleus CI all channels have the same stimulation rate. Lowering the stimulation rate reduces the power level and thus improves the battery life.

[redacted]

Neural elements

[redacted]

4.2 Findings of Previous Nonclinical and Clinical Studies

4.2.1 Nonclinical Data

Safety studies on cats and guinea pigs have shown that chronic stimulation with wide PW is safe (McCreery et al., 1988, 1990).

4.2.2 Clinical Data

Stimulation rate: Big data analysis of 39885 CI recipient MAPs from the USA showed that the majority of recipients (84.85%) were fitted with the default stimulation rate of 900Hz, suggesting that clinicians tend to choose the default parameters unless there are specific reasons not to choose them. When the stimulation rate was changed however, the most popular stimulation rate chosen was 500Hz (8.42%) (Maruthurkkara & Bennett, 2022).

A review of literature (Carpenter, 2018) identified 25 articles that evaluated the relationship between rate of electrical stimulation and perceptual outcomes in CI recipients out of a total 653 articles. The literature review

showed that published clinical studies report no significant group mean effects of stimulation rate on hearing performance outcome. The author concluded that unless an individual recipient exhibits performance or preference in favour of higher rates, it would be appropriate to use stimulation rates as low as 500 pps.

Pulse width: Busby et al., (1993) showed that when PW is changed there was no difference in modulation detection or discrimination abilities. Zhou et al., (2020) demonstrated in an electrophysiological study that wider PW has a narrower spread of excitation compared to an equally loud pulse with a narrow PW. The narrower spread of excitation may be beneficial for speech perception.

Interphase gap: Psychophysical and electrophysiological studies have shown that as the IPG is increased, there is a reduction of T and C levels and an increase in the neural response amplitude and the electrical dynamic range (Carlyon et al., 2005; McKay & Henshall, 2003; Schvartz-Leyzac & Pfingst, 2016). Some authors have concluded that wider IPG increases the efficiency of the neural excitation.

[redacted]

4.3 Study Rationale

The default parameters used for creating MAPs in monopolar mode are stimulation rate of 900 Hz, a PW of 25µs, and an IPG of 8µs. Table 2 lists in increasing order of benefit three MAP parameter combinations that aim to improve the battery life:

[redacted]

These MAP parameter combinations may better ensure that the MAP levels are within compliance limits and improve battery life. Several studies, summarised in section 4.2.2, have evaluated different features independently to demonstrate their safety and effectiveness. It is of interest to evaluate combinations of these parameters and their effect on speech perception so that they may be implemented in future sound processors. Since LP1 utilises the same stimulation rate, it is the easiest to implement as a low-power strategy. Thus, the comparison of the default with LP1 in quiet and in noise are the two primary objectives for

this study. Since LP2 uses a lower rate and LP3 uses DE mode along with a lower rate, although they have greater battery life saving potential, they are harder to implement as a low power option as they produce a greater change in the sound quality. Thus, the comparison of LP1 with LP2 and LP3 forms the second primary objectives for this study. If the LP3 program provides suboptimal hearing performance, it may still be used as a low-power program on days when the CI recipient desires extended battery life and is willing to trade off hearing performance. However, in those instances, switching from one program to another (LP2 to LP3) will need to be acceptable. Thus, the ease of switching from LP2 to LP3 is a secondary objective in this study. We are also interested in hearing performance comparisons between LP2 and LP3 and real-world feedback, and thus they form the exploratory objectives of the study.

Table 2: MAP parameter combinations to improve battery life.

This clinical study aims to confirm the in-booth performance of MAPs that use wider PW with 900Hz stimulation rate and MAPs with a combination of low rate (500Hz), wide PW (100µs), and wider IPG (12µs) in dual-electrode mode, compared with the default stimulation parameters currently used in Custom Sound 7.0. This study will build on the evidence collected in previous clinical studies listed in section 4.2.2.

5 MEDICAL DEVICE INFORMATION

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

The IMD for this investigation is dual-electrode mode configuration of stimulation mode in the firmware of the Nucleus 7 (CP1000), Nucleus 8 (CP1110) and Kanso 2 (CP1150) sound processors outside of the functionality of the commercial system. Dual-electrode mode programs will be created using research software called Cochlear Device Interface Tool (CDI Tool). The investigational ACE MAPs include changes in electrical stimulation parameters such as stimulation rate, PW, stimulation mode and IPG listed in Table 2. This investigational MAPs are used solely for the purpose of clinical investigation. Figure 3 shows a screenshot of the CDI Tool software.

Figure 3: Screenshot of Cochlear Device Interface Tool (CDI Tool).

The clinical hardware used in this study includes a computer with the research CDI Tool software, a commercially available programming pod, and a commercially available CP1000, CP1110 and CP1150 sound processor. The computer is connected to the programming pod, which is then connected to the sound processor.

The development of the research tool (CDI) followed a design control process that is part of Cochlear's ISO13485 compliant quality management system. The research tool has been verified for safety and technical correctness before use in a human trial. The research software tool underwent safety and performance testing according to Cochlear product risk management procedures, in accordance with EN ISO 14971, Medical devices – Application of risk management to medical devices (ISO 14971, 2004) standard. The overall residual risks associated with the investigational devices are acceptable. All risk reduction measures shown in the essential requirements document have been implemented into the final design and verified to be effective.

Subjects will use the MAPs created using the research tool exclusively for the duration of the study. The research tool will be clearly labeled as such on the personal computer. The build number will be documented in the tracking forms, such as the Software Tracking Form (1302326), as mentioned in section 12 of this document. The investigator will undergo training on how to use the IMD and the research tool, and the completion of this training will be recorded in a training log.

5.2 Identity and Description of the Comparator

The commercially available ACE coding strategy programmed with the default 900Hz stimulation rate will serve as the comparator. The investigator will use CDI Tool to create the comparator MAP. MAPs will be written to the commercially available CP1000, CP1110 and CP1150 sound processors.

5.3 Accessory Device Requirements

Not applicable.

6 OBJECTIVES

Table 3: Schematic overview of the objectives

	Primary objective	Secondary objective	Exploratory objective
Quiet testing	Default Vs LP1	LP1 Vs LP2 LP1 Vs LP3	LP2 Vs LP3
Noise testing	Default Vs LP1	LP1 Vs LP2 LP1 Vs LP3	LP2 Vs LP3
Questionnaire	-	LP2 Vs LP3 (SAR)	LP1 Vs LP3 (SSQ)

6.1 Primary Objectives

1) To evaluate speech perception in quiet with default and LP1[1] MAPs.
2) To evaluate speech perception in noise with default and LP1 MAPs

6.2 Secondary Objectives

1) To evaluate speech perception in quiet with LP1 and LP2[2] MAPs
2) To evaluate speech perception in noise with LP1 and LP2 MAPs
3) To evaluate speech perception in quiet with LP1 and LP3[3] MAPs.
4) To evaluate speech perception in noise with LP1 and LP3 MAPs
5) To evaluate acceptance of switching between LP2 and LP3 MAPs

6.3 Exploratory Objectives

1) To evaluate speech perception in quiet with LP2 and LP3 MAPs
2) To evaluate speech perception in noise with LP2 and LP3 MAPs
3) To evaluate adult cochlear implant subjective hearing performance and sound quality with LP1 and LP3 MAPs

[redacted]

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

This is a prospective, single centre, single-blind, single-subject repeated measure investigation, of hearing outcomes when adult CI recipients are programmed with different rates or pulse-widths along with dual-electrode mode compared with standard programming parameters.

The subjects include adults aged 18 years and older with sensorineural hearing impairment who are current users of a Nucleus CI system. Subjects will be screened, and 20 eligible subjects will be recruited in the clinical investigation from a single investigational site located in Australia. After enrolment, ACE MAPs will be created with the parameters in Table 2 using CDI tool in visit 1.

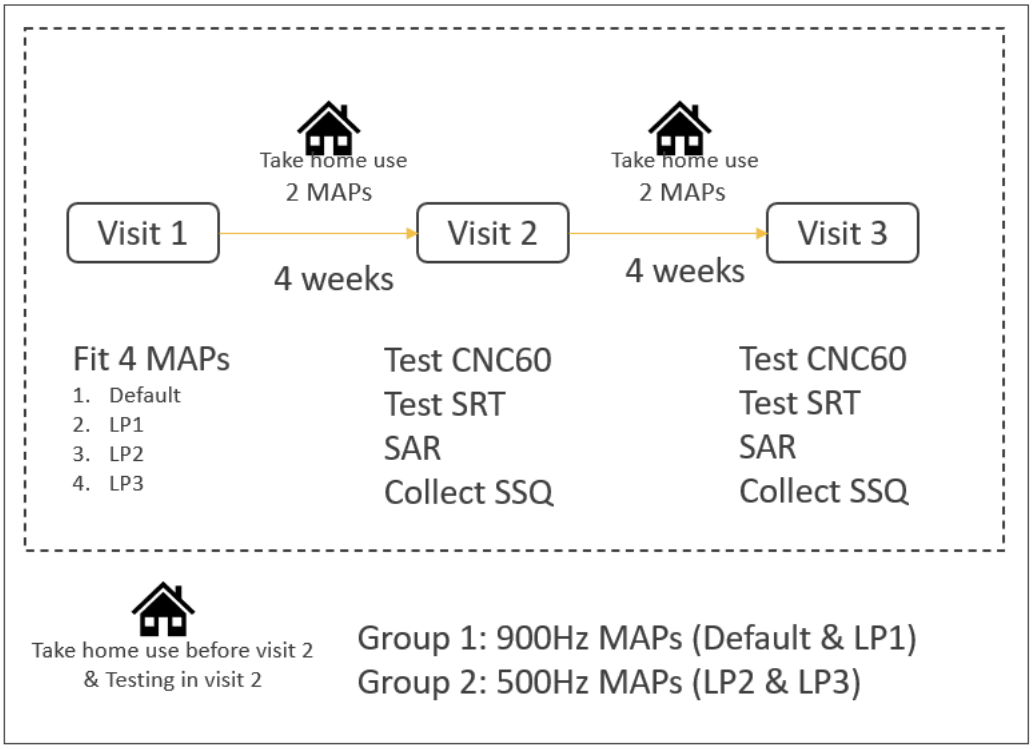

Figure 4: Simplified schematic of study procedures

Subjects will attend a minimum of three scheduled study visits over an eight-week study period as described in the CIP Schedule of Events (Section 3). Additional study visits may be scheduled if all study procedures could not be completed during a scheduled visit. At study visits, subjects will undergo hearing assessments and complete questionnaires. The primary objectives are to determine the hearing performance of LP1 MAP compared to default MAP at the end of the study, as assessed by speech perception performance. Safety will be assessed by recording and summarising all Adverse Events (AE)/ Adverse Device Effects (ADE) and Device Deficiencies (DD). No data monitoring committee will be used for this clinical investigation. All subjects will attend an end-of-study visit at the time they complete the study.

7.1.1 Design Rationale

Subjects

- Only CI recipients implanted with the CI500 series, CI600 series or Freedom series CIs in one or both ears are included as the CDI tool only supports these CIs.
- Hearing ability and the MAPs undergo significant changes in the first months after implantation. Thus, CI recipients with at least three months experience with their CI will be enrolled so that any changes in their hearing function do not act as confounding variables.
- Only adult CI recipients rather than children have been chosen as the study population due to their ability to compare MAPs, in and outside of the booth. Additionally, performance benefits achieved by adults can generally be extrapolated to younger age groups, avoiding the need to recruit this vulnerable population.
- Only subjects who are able to score 20% or more for English CNC words presented at 60dB SPL RMS with CI alone in the test ear will be recruited to avoid floor effects.
- Only subjects willing and able to provide written informed consent will be enrolled to be compliant with ISO 14155.
- Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling or Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of this investigation will be excluded to avoid enrolment of a vulnerable population.
- Only subjects with all 22 electrodes active in the MAP used regularly will be enrolled as all 22 electrodes are required to create a MAP with dual-electrode mode that is comparable across subjects.

Blinding

- Blinding of the study subject will be undertaken, to reduce any bias. Subjects will not be told which MAP will be loaded in the sound processor for take home use and which MAP order to be tested at Visit 2 and Visit 3.
- There will be no blinding of the study investigators.

Visit window

- The stimulation rate and dual-electrode mode is likely to be novel to the study subjects. Subjects will be asked to use MAPs with 900Hz (default & LP1) and 500Hz (LP2 & LP3) for at least four weeks so that they have sufficient experience with the MAP prior to the speech perception tests with those MAPs.

Outcome measures

- CNC words: Speech perception in quiet will be measured using recorded CNC monosyllabic words (Peterson & Lehiste, 1962) at 60dBSPL from S0 position. CNC words in quiet at 60dB SPL presentation level will be used to emulate conversational levels. The goal of speech perception assessment in quiet is to compare % words correct for each of the conditions. This outcome measure is routinely used in clinical practice and research studies.

- Australian Speech Test In Noise (AuSTIN): Speech perception in noise will be measured using the AuSTIN (Dawson et al., 2013), which is a test that uses recorded BKB like target sentences. The goal of the speech perception test in noise is to provide the SNR for 50% speech intelligibility. AuSTIN speech perception test will be used to evaluate hearing in noise ability in the sound booth. The test is used routinely in clinical practice and research studies.
- The Speech and spatial qualities questionnaire (SSQ12) is designed to measure a range of hearing disabilities across several domains (Noble et al., 2013) in real world conditions. This questionnaire is routinely used in clinical practice and research studies.
- Switching acceptability rating (SAR): The SAR is an unvalidated rating scale designed to gather subjective feedback on the sound quality differences between two programs and assess the difficulty in acclimating to a new MAP after using it for 10 minutes to listen to recorded and live speech (Appendix 1).
- Clinician log: The clinician log will capture the MAP changes made by the clinician in response to the subject's feedback.
- Comparisons will be made within-subject with repeated measures for each of the MAPs to be evaluated so that any subject specific variable that can potentially affect the outcomes has equal effect on all conditions.
- Counterbalancing of the test order will be undertaken where possible to limit the influence of order effects on results.

7.2 Subjects

Written, informed consent must be obtained from the subject before any study procedures are initiated. Eligibility of subjects must be supported by a CNC word test score at 60dB (available within 12 months prior to enrolment or conducted at screening) to confirm that the subject is able to score 20% or more in the ear to be studied. Custom Sound data can be used to confirm age, suitable implant type, duration of CI use, and number of active electrodes.

7.2.1 Inclusion Criteria

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

1) Implanted with the CI600 Series (CI612, CI632, CI622, CI624), CI500 Series (CI512, CI513, CI532, CI522) or Freedom Series (CI24RE(CA), CI24RE(ST), CI24RE(CS), CI422)

2) At least three months after activation of the cochlear implant.

3) Eighteen years or older at the time of consent.

4) User of 900Hz ACE (Advanced Combination Encoder) strategy MAP.

5) Score of 20% or more for CNC words presented at 60dBSPL with CI alone in the test ear.

6) Fluent speaker in English.

7) Willing and able to provide written informed consent.

7.2.2 Exclusion Criteria

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

1) One or more electrodes turned off in the MAP used regularly.
2) Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator.
3) Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.
4) Cochlear employees or employees of Contract Research Organisations or contractors engaged by Cochlear for the purposes of this investigation.
5) Current participation, or participation in another interventional clinical study/trial in the past 30 days, involving an investigational drug or device (unless the other investigation was/is a Cochlear sponsored investigation and determined by the investigator or Sponsor to not impact this investigation).

7.2.3 Number of Subjects Required

Twenty subjects will be enrolled in the study to meet sample size calculation requirements stated in section 9.4 with the allowance for dropout rate (25%) and to ensure balanced subgroups.

7.2.4 Vulnerable Populations

Not applicable for the current clinical investigation.

7.2.5 Recruitment and Study Duration

The following subject status definitions apply:

- Enrolled: A subject that has signed the Informed Consent form for the study.
- Screen Fail: An Enrolled subject that has been determined to not meet one or more eligibility criteria.
- Participated: Subjects who have met eligibility criteria and have commenced visit 1 procedures.
- Discontinued: An Enrolled subject who withdrew consent, was discontinued by the Investigator or Sponsor before the expected End of Study visit or lost to follow-up. Discontinued subjects may still have safety follow up data collection until their scheduled End of Study visit, for reasons described in section 7.2.6.
- Completed: Enrolled subjects who complete the required treatment and visit schedule.

The recruitment period for the clinical investigation is estimated to be seven months from the time of first subject consent to recruitment of the last subject. This is to allow the replacement of any subjects who withdraw from the study.

The expected minimum duration of each subject's participation in the clinical investigation, is eight weeks, from the time of informed consent through to the End of Study when devices are returned. The anticipated total duration of the clinical investigation is 12 months.

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

7.2.6 Criteria and Procedures for Subject Withdrawal

Subjects can decide to withdraw from the investigation at any time. The Investigator shall ask the reason(s), however subjects have the right to withhold their reason if preferred. The reason for withdrawal should be documented in the subject's source files and the case report form (CRF), if provided.

The Investigator or Sponsor may also decide to withdraw a subject from the clinical investigation or stop the use of the investigational device if it is considered to be in the subject's best interests.

Subject withdrawal may be for any of the following reasons:

- Adverse Event (AE)
- Device Deficiency (DD)
- CIP or GCP deviation
- Subject withdrew consent
- Subject lost to follow-up
- Subject death
- Sponsor decision
- Investigator decision
- Other (specify)

If subject withdrawal is due to problems related to the IMD safety or performance, the Investigator shall ask for the subject's permission to continue in safety follow up (for example, adverse events and device deficiencies) until their scheduled End-of-Study visit.

If a subject is lost to follow-up, every possible effort must be made by the study site personnel to contact the subject and determine the reason for discontinuation. At least 3 separate attempts taken to contact the subject must be documented.

Participating subjects who are withdrawn/discontinued before the data for primary and secondary endpoints have been collected, may be replaced to meet the minimum sample size criteria or to maintain counterbalancing between the groups.

7.2.7 Randomisation Procedures

Subjects will be randomly allocated to one of four groups. Programming of sound processors for take home use and test order during visits 2 and 3 will be performed as per the randomisation table (Table 4).

Table 4: Randomisation table

	Take home programs	Visit 2 test order	Take home programs	Visit 3 test order
Group 1A	P1: Default P2: LP1	Test 1: Default Test 2: LP1	P1: LP2 P2: LP3	Test 1: LP2 Test 2: LP3
Group 1B	P1: LP1 P2: Default	Test 1: LP1 Test 2: Default	P1: LP3 P2: LP2	Test 1: LP3 Test 2: LP2
Group 2A	P1: LP2 P2: LP3	Test 1: LP2 Test 2: LP3	P1: Default P2: LP1	Test 1: Default Test 2: LP1
Group 2B	P1: LP3 P2: LP2	Test 1: LP3 Test 2: LP2	P1: LP1 P2: Default	Test 1: LP1 Test 2: Default

7.2.7.1 Blinding Procedures

For in-booth speech perception testing, the test order will not be revealed to the study subject. The counterbalancing procedures will be used to ensure that there is a balanced order of test conditions.

7.2.8 Post-investigation Medical Care

As this clinical investigation is non-surgical in nature, no specific medical care will be provided for the subjects after the clinical investigation has been completed. All IMD management during the study will be done by the study investigators. Subjects will be able to see their regular clinicians when wearing their own sound processors. At the end of the study, subjects will return all loaner and investigational devices to the investigator and return to using their own sound processors programmed with commercial programming software versions. Subjects will continue to be clinically managed by their regular clinician according to their clinic's standard practice after the clinical investigation has been completed.

7.3 Evaluations and Procedures

7.3.1 Screening/eligibility

- **Informed consent:** Informed consent will be obtained as per procedures detailed in section 10
- **Eligibility:** The subject's Custom Sound data will be reviewed to assess the eligibility in terms of age, implant type, number of active electrodes and duration of CI experience. Historical CNC word test results (60dB) will be reviewed to ascertain eligibility. If historical data in the last 12 months is not available, then one list of CNC words at 60dB presentation level will be administered on each implanted ear to determine eligibility after informed consent is obtained. For bilateral CI recipients, the better ear in terms of CNC word scores will be chosen as the test ear. The subject's preferred ear will be chosen in the event that both ears are eligible and have the same test scores for CNC words.

- **Standard CRFs:** CRFs including demographics, eligibility, medical, hearing and device history, concomitant medications and device exposure will be completed.

7.3.2 Performance/Effectiveness

Section 3 shows the overall schedule of events to be followed in this study. Figure 4 shows a simple schematic of the study procedures. Below each visit procedures are provided in greater detail. The subjects will be randomly allocated to groups 1A, 1B, 2A or 2B.

Visit 1:

- **Mapping:** Four MAPs using parameters listed in Table 2 will be created. The default MAP will be created by measuring T-levels on electrodes 22, 16, 11, 6, 3, and 1. If required, additional T-levels may be measured by the clinician. The Hughson-Westlake method will be used for T-level measurement, aiming for two out of three detections on an ascending run with step sizes of 2 CL up and 4 CL down. Two beeps will be used to determine the T-levels. The C-level profile will use the T-level profile as the starting point. C-levels will be raised globally in live mode until ongoing conversational speech is comfortably loud. The C-levels will be balanced in overlapping groups of three channels. Additional T/C level modifications may be made by the clinician to address any sound quality issues. The T and C levels from the default MAP will be converted to create the LP1, LP2 and LP3 MAPs. For LP3, the T and C levels for each dual channel will be configured to be an average of the two single electrodes comprising the channel. The clinician may change the levels as required to ensure that the LP MAPs are acceptable and have the same loudness as the default MAP by global C-level adjustments and ensuring loudness balance across channels. Loudness balancing will be performed to ensure all MAPs are equally loud. The investigators will be provided hands on training by the sponsor on the use of CDI Tool research software for the creation of the MAPs.
- **Clinician log:** The clinicians creating the different MAPs will be asked to complete a log (Appendix 2) to record the steps undertaken during creation and optimisation of the different MAPs. The log will capture the clinician's action and the feedback from the CI recipient. To aid in the completion of the log, screen recording with audio recording will be captured.
- **Preparation of take-home sound processor:** Group 1 will be provided with 900Hz MAPs (Default and LP1), and group 2 will be provided with 500Hz MAPs (LP2 and LP3) as per the randomisation table (Table 4). The SmartSound environments in the frequently used program in their own sound processor will be replicated in the study sound processor with the exception of automatic forward focus (SCAN2FF). Subjects using a SCAN2FF program in their own sound processor will be provided a SCAN2 program with user-controlled ForwardFocus enabled.
- **Issue of SSQ12:** The SSQ12 questionnaire will be issued, and the subjects will be counselled on how to complete the questionnaire as needed. The subjects will be asked to rate their ability to hear speech in a variety of competing contexts during their take home period. Subjects are also asked about their spatial hearing abilities including the impact of direction, distance and movement associated with spatial hearing.

- **Counselling for take home use:** Subjects will be asked to switch from program 1 to program 2 on a daily basis so that they acclimate to both programs and to get equal opportunity to use both programs during the take home period. Subjects who typically used the SCAN2FF program prior to enrolment will be asked to use user-controlled ForwardFocus during the take home period.
- **Standard CRFs:** CRFs including concomitant medications, adverse events and device deficiencies will be completed.

Take home use:

- Subjects will be asked to use two MAPs for four weeks. The subjects will be asked to use P1 on day 1, P2 on day 2, P1 on day 3 etc.
- Subjects will be asked to complete the SSQ12 in the fourth week of take home use.

Visit 2:

- **Collection of SSQ12:**
- **Acclimatization:** Subjects will be asked to use the specified test MAP for a period of minimum 10 minutes and listen to live or recorded speech to acclimate to two conditions prior to speech perception testing. Contralateral device will be turned off (if applicable).
- **SAR:** The subjects will be asked to provide responses to the questions in the SAR as soon as they have switched to the new MAP at the end of the acclimatisation period.
- **CNC word test (60dB):** Two lists with 50 words each will be administered per condition. The contralateral ear will be plugged. The test order will be determined using the randomisation table (Table 4)
- **AuSTIN sentence test:** Both recorded speech and noise (adaptive four talker babble noise) will be presented from 0 degrees azimuth (S0N0). The signal level will be fixed at 65 dB SPL. One practice list will be administered at the beginning of the session to overcome learning effects. Two lists with 20 sentences each will be administered per condition. If the standard deviation (SD) for any list exceeds 4.12, then the run will be considered as invalid and additional list will be administered. The contralateral ear will be plugged.
- **Loading MAPs to processors**: CDI Tool will be used to load the test MAPs into a study sound processor for take home use as per the randomisation table (Table 4).
- **Issue of SSQ12:** The SSQ12 questionnaire will be issued, and the subjects will be counselled on how to complete the questionnaire as needed.
- **Standard CRFs:** CRFs including concomitant medications, adverse events, device deficiencies and device exposure will be completed.

Take home use:

- Subjects will be asked to use two MAPs for four weeks. The subjects will be asked to use P1 on day 1, P2 on day 2, P1 on day 3 etc.
- Subjects will be asked to complete the SSQ12 in the fourth week of take home use.

Visit 3:

- **Collection of SSQ12:**
- **Acclimatization:** Subjects will be asked to use the specified test MAP for a period of minimum 10 minutes and listen to live or recorded speech to acclimate to the two conditions prior to speech perception testing. Contralateral device will be turned off (if applicable).
- **SAR:** The subjects will be asked to provide responses to the questions in the SAR as soon as they have switched to the new MAP at the end of the acclimatisation period.
- **CNC word test (60dB):** Two lists with 50 words each will be administered per condition. The contralateral ear will be plugged. The test order will be determined using the randomisation table (Table 4)
- **AuSTIN sentence test:** Both recorded speech and noise (adaptive four talker babble noise) will be presented from 0 degrees azimuth (S0N0). The signal level will be fixed at 65 dB SPL. One practice list will be administered at the beginning of the session to overcome learning effects. Two lists with 20 sentences each will be administered per condition. If the SD for any list exceeds 4.12, then the run will be considered as invalid and additional list will be administered. The contralateral ear will be plugged.
- **Standard CRFs:** CRFs including concomitant medications, adverse events, device deficiencies and device exposure will be completed.

Additional visits

- Additional visits may be conducted in case any of the procedures in any of the visits could not be completed.

End of study

- **Return of devices:** The study devices will be collected back from the subjects.
- **Programming own device:** The subject's own sound processor will be checked to ensure that it contains their own MAPs and is programmed with the commercial version of Custom Sound fitting software.

7.3.3 Safety Evaluations and Procedures

The risks and anticipated ADEs for the IMD, as identified in Sections 8.2 and 8.3 of the CIP, will be assessed in the clinical investigation via reporting of all AEs/ADEs from the time of first subject first visit until last subject last visit.

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

7.3.3.1 Concomitant Medication and Therapies

All concomitant medical treatments will be collected as part of this study.

7.4 Equipment Used for Evaluations and Procedures

7.4.1 Software

Speech testing in quiet and noise will be performed using the SRT software. The printed test report will be considered as source data. The electronic data generated from the tests will be stored in a secure network drive at the site.

The programming will be performed using CDI Tool and Custom Sound 7.0. The electronic data generated from the programming will be stored in a secure network drive at the site.

A commercially available screen recording software will be used for screen recording to aid the completion of the clinician log.

7.4.2 Sound room equipment

Speech perception performance in quiet and in noise will be assessed using a loudspeaker configuration with the speech from the front (S0) and speech and noise from the front (S0N0) respectively.

There will be defined locations for the loudspeakers and subject within the test environment. The loudspeakers will be located at head height for a seated subject (reference point). The distance of the loudspeaker from the reference point will be fixed.

To ensure accurate and reliable results, the equipment in the sound room will undergo an annual calibration. Additionally, a quick calibration check will be performed routinely to maintain the quality of the equipment.

7.4.3 Questionnaires

Paper-based questionnaires will be used to gather responses on SSQ12 from subjects and to be entered into EDC by site staff.

7.5 Sponsor Role in Conduct of the Clinical Investigation

Sponsor and investigator roles are assumed by Cochlear employees.

This clinical investigation will be conducted by an internal site. Internal sites are clinical research facilities owned and operated by Cochlear. The internal site at Cochlear in Sydney consists of a small team of Investigators, trained as clinical audiologists, to execute this research activity including subject recruitment, programming and study evaluations and data entry into eCRF. Investigators are qualified audiologists familiar with CI development, surgery and programming. The list of authorised personnel and their roles will be recorded in the delegation log. Investigators' trial materials, programming and testing rooms (sound booths) will only be accessible to the study team and will be securely separated from rest of the organisation.

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

8.1 Anticipated Clinical Benefits

There is no anticipated clinical benefit for subjects. The investigational MAPs and research tools will be used within the study period only. The indirect benefit could be that in future, through this clinical investigation, Cochlear may bring product improvements to the market that improve battery life for CI recipients.

8.2 Anticipated Adverse Device Effects

The subjects of this clinical investigation are already implanted with a commercially available Nucleus implant device, independent of this study. No medication will be prescribed for the study.

The expected risks with use of commercially available CP1000, CP1110 and CP1150 sound processors are described in user guides.

The investigation is focused solely on hearing therapy, specifically fitting. The electrical stimulation can be different from their own sound processor device due to changes in the MAPs. Subjects will have access to their standard baseline MAP on their own sound processor that they can return to at all times.

8.3 Risks Associated with Participation in the Clinical Investigation

Potential clinical risks associated with participation in the clinical investigation include:

Uncomfortably loud stimulation: The subjects will undergo programming of their CI using research software. Fitting is a key step of the study, and the associated risk is not exceeding the risk during normal clinical handling of a CI. To mitigate this risk, the same level of control measures is implemented in the research software as in the standard commercial clinical fitting software. Furthermore, the fitting is conducted or overseen by an experienced clinician.

Non-auditory stimulation: In rare cases, stimulation of the CI can lead to stimulation of non-auditory structures such as the facial nerve. It is a standard hazard in clinical management of hearing implant users. It is essentially controlled during fitting of the implant. Also, this will always be known already from the clinical experience with the subject and can be prevented by e.g., stimulating just below the level when the non-auditory stimulation occurs or by deactivating specific electrode channel(s). Also, the fitting is conducted or overseen by an experienced clinician. The associated risk is not exceeding the normal clinical handling of a CI.

Wrong stimulation delivered (within safety limits): It is conceivable that due to an implementation error in research firmware or software a wrong stimulus would be delivered. Through thorough formal verification the probability that unintended electrical pulses would be delivered is low.

Sub-optimal fitting of the device resulting in sub-optimal performance: It is possible that investigational MAPs result in a decline of hearing outcomes. It is well known that some types of changes to a MAP may lead to an acute minor decline in hearing outcomes. As the CI user adapts to the new sound quality, this decline is

often temporary. But in the worst case a user may not adapt. In this study a CI clinician will be available to provide hearing care, and address reports of degraded performance. In the case of prolonged observed systematic decrease in performance the particular test set-up/condition can be halted. Subjects will also have access to their standard baseline MAP on their own sound processor that they can return to at all times. Again, this risk is similar to the risk in normal clinical management.

After the study has been finished, the patients will return to their original/preferred MAP using their own sound processor.

It is expected that there may be increased inconvenience and potential discomforts to study subjects, but no potential risk of physical or psychological harms have been identified. In summary, the risks involved with the clinical investigation procedures are not substantially different from the risks associated with a normal clinical session with CI users.

8.4 Risk Mitigation

The investigational software and firmware to be assessed will undergo safety and performance testing according to Cochlear product risk management procedures, in accordance with EN ISO 14971 (Medical devices – Application of risk management to medical devices) standards.

The following will be performed during the clinical investigation to mitigate the risks identified above:

- Detailed study procedure instructions are provided to the investigator to mitigate the risks of inappropriate use of the investigational device.
- Investigators are trained to avoid over-stimulation and/or non-auditory stimulation and the recipient has the possibility to remove the coil of the sound processor from their head to stop stimulation.
- Subjects may revert to using their own Nucleus sound processor programs, if in a situation where it is felt that performance is not sufficient with the new program(s).

All reported ADEs and DDs will be regularly reviewed by the Sponsor's Clinical Review Board for the duration of the study to facilitate early detection and appropriate intervention if events are unanticipated with respect to incidence, severity, or outcome.

8.5 Benefit-to Risk Rationale

The risks involved with the investigational devices to be evaluated under this clinical investigation are not substantially different from the risks associated with normal CI users, and the risks involved with the clinical investigation procedures are not substantially different from the risks associated with a normal clinical session for CI users.

The potential temporary inconveniences and discomforts associated with participation in this investigation is proportional to the indirect benefits, as described in section 8.1.

9 STATISTICAL CONSIDERATIONS

9.1 General Considerations

See sections 9.2 to 9.8 for statistical considerations.

9.2 Endpoints

For speech in quiet (CNC) endpoints, two lists of words will be measured per sound processor condition, and the two percentage words correct values will be averaged to produce a single value per condition, per subject.

For speech in noise (AuSTIN) endpoints, two lists of sentences will be measured per sound processor condition, and the two dB SRT values will be averaged to produce a single value per condition, per subject.

Each SSQ questionnaire which includes 12 questions will be measured per sound processor condition per person. The score is a continuous numeric score, and a single value will be recorded per question. For the SSQ12 endpoint, the total scores will be compared.

9.2.1 Primary Endpoints

1) Paired difference in percentage CNC Words correct between default and LP1 MAPs in quiet setting

2) Paired difference in dB SRT (AuSTIN) between default and LP1 MAPs in noise

9.2.2 Secondary Endpoints

1) Paired difference in percentage CNC Words correct between LP1 MAP and LP2 MAP in quiet setting

2) Paired difference in dB SRT (AuSTIN) between LP1 and LP2 MAPs in noise

3) Paired difference in percentage CNC Words correct between LP1 and LP3 MAPs in quiet setting

4) Paired difference in dB SRT (AuSTIN) between LP1 and LP3 MAPs in noise

5) Ratings on switching acceptability rating

9.2.3 Exploratory Endpoints

1) Paired difference in percentage CNC Words correct with LP2 and LP3 MAPs

2) Paired difference in dB SRT (AuSTIN) between LP2 and L3 MAPs

3) Paired difference in global SSQ12 scores after experience with LP1 and LP3 MAPs

9.3 Hypotheses

For the non-inferiority test of CNC words, the 95% CI (alpha=0.025 one-sided) for the mean paired difference will be estimated. If the lower limit of the 95% CI of the mean paired difference is above -10%, the treatment condition is regarded as non-inferior to the control on that measure.

For the non-inferiority test of SRT sentences for both primary and secondary endpoints, the 95% CI (alpha=0.025 one-sided) for the mean paired difference will be calculated. If the upper limit of the 95% CI of the mean paired difference is lower than 1dB, the treatment condition is regarded as non-inferior to the control on that measure.

9.3.1 Primary Hypotheses

Primary endpoint 1: Paired difference in percentage CNC Words correct between default and LP1 MAPs in quiet setting

H0: Words in quiet (60 dB CNC words) scores (% words correct) with the LP1 MAP are inferior to those with the default MAP.

LP1 – default < -10%

H1: Words in quiet (60 dB CNC words) scores (% words correct) with the LP1 MAP are non-inferior to those with the default MAP.

LP1 – default > -10%

Primary endpoint 2: Paired difference in dB SRT (AuSTIN) between default and LP1 MAPs in noise

H0: Sentence in noise scores (dB SRT) with the LP1 MAP are inferior to those with the default MAP.

LP1 MAP – default ≥ 1 dB (NB: higher SRT scores represent poorer performance)

H1: Sentence in noise scores (dB SRT) with the LP1 MAP are non-inferior to those with the default MAP

LP1 MAP – default < 1 dB

9.3.2 Secondary Hypotheses

Secondary endpoint 1: Paired difference in percentage CNC Words correct between LP1 MAP and LP2 MAP in quiet setting

H0: Words in quiet (60 dB CNC words) scores (% words correct) with the LP2 MAP are inferior to those with the LP1 MAP

LP2 – LP1 < -10%

H1: Words in quiet (60 dB CNC words) scores (% words correct) with the LP2 MAP are non-inferior to those with the LP1 MAP

LP2 – LP1 > -10%

Secondary endpoint 2: Paired difference in dB SRT (AuSTIN) between LP1 and LP2 MAPs in noise

H0: Sentence in noise scores (dB SRT) with the LP2 MAP are inferior to those with the LP1 MAP

LP2 MAP – LP1 ≥ 1 dB (NB: higher SRT scores represent poorer performance)

H1: Sentence in noise scores (dB SRT) with the LP2 MAP are non-inferior to those with the LP1 MAP

LP2 MAP – LP1 < 1 dB

Secondary endpoint 3: Paired difference in percentage CNC Words correct between LP1 and LP3 MAPs in quiet setting

H0: Words in quiet (60 dB CNC words) scores (% words correct) with the LP3 MAP are inferior to those with the LP1 MAP

LP3 – LP1 < -10%

H1: Words in quiet (60 dB CNC words) scores (% words correct) with the LP3 MAP are non-inferior to those with the LP1 MAP

LP3 – LP1 > -10%

Secondary endpoint 4: Paired difference in dB SRT (AuSTIN) between LP1 and LP3 MAPs in noise

H0: Sentence in noise scores (dB SRT) with the LP3 MAP are inferior to those with the LP1 MAP

LP3 MAP – LP1 ≥ 1 dB (NB: higher SRT scores represent poorer performance)

H1: Sentence in noise scores (dB SRT) with the LP3 MAP are non-inferior to those with the LP1 MAP

LP3 MAP – LP1 < 1 dB

Secondary endpoint 5: Ratings on switching acceptability rating.

There are no hypotheses for this endpoint.

9.3.3 Exploratory Hypothesis

There are no exploratory hypotheses.

9.4 Sample Size Determination

This study is a non-inferiority design, and sample size calculation was based on non-inferiority tests for CNC word scores and SRT (Speech Recognition Threshold) scores.

To reject the null hypothesis of inferior CNC Words correct in quiet (60 dB) scores, a sample size of 14 will provide more than 90% power to detect non-inferiority of CNC word scores and 90% power to detect non-inferiority of SRT with the following parameters:

- A clinically important difference value of 10% for CNC words and 1 dB SRT for AuSTIN. This margin is based on clinical consensus.
- A SD of change or difference scores of 6.914% for CNC words and 1.037 dB for AuSTIN. The expected standard deviation of difference scores for CNC words was based on a previous dual electrode mode study (CRC 5523) on the relevant endpoints.
- A significance level $\alpha = 0.025$ (one-tailed).

There are four subgroups in the randomisation table (Table 4); to ensure equal number of subjects in each subgroup a minimum of sample size of 16 (or a higher multiple of 4) is required. Twenty subjects will be enrolled in total to allow for any unforeseen subject withdrawal with a possible attrition rate of 25% and to ensure equal number of subjects in the four subgroups. Replaced subjects will be recruited if the minimum sample size of 16 could not be met due to subject withdrawal or loss to follow up.

9.5 Analysis Populations

The analysis of the primary endpoint will be based on the Intent-To-Treat (ITT) and Per Protocol (PP) analysis populations in order to support a conclusion of non-inferiority. The inclusion of both ITT and PP populations has been chosen to assess the robustness of the study results and the consistency of the study measures under different analysis populations.

This study has a non-inferiority design; therefore, the primary analysis will be based on the PP population.

For cases in which the ITT and PP populations lead to the same conclusions and final interpretations about the LP MAP effect, the results will be considered to not be influenced by underlying factors such as missing data and protocol deviations, and the results would be considered to be robust and consistent under different analysis populations. A statement to reflect this will be included in the CIR.

For cases in which the ITT and PP populations lead to different final interpretations or conclusions, all of the results will be reported and the differences in outcomes will be identified and explored.

Intent-to-Treat Population

The Intent-to-Treat Population will include all subjects who receive the MAPs and have at least one set of paired MAPs measurements from any endpoint, regardless of protocol deviations and missing data.

Per Protocol Population

The Per Protocol Population will include all subjects who receive the MAPs and have at least one set of paired MAPs measurements without major protocol deviations from any endpoint. Major deviations will be defined and documented at the clean file meeting before data base lock.

It is possible that a LP MAPs has not been administered in the intended counterbalanced order of presentation. It is also expected that the sequence and period effects are minimal in this study if any. This study is not a full cross-over design, so period and sequence effects will not be assessed, without the consequence to bias the study conclusion.

Safety Population

The Safety Population will include all subjects who used the investigational MAPs. The Safety Population will be used for the safety data analysis.

9.6 Endpoint Analyses

For all hypothesis testing to be performed on primary and secondary endpoints, the overall type I error rate will be maintained via a gatekeeping approach whereby statistical tests will proceed in order as stated under the section 9.3 until a non-significant test is obtained, at which point, formal testing for the purposes of labelling claims will cease. However, summary statistics on the remaining endpoints will still be performed.

9.6.1 Primary Endpoint Analyses

SRT sentence scores in noise and words in quiet scores at different speech testing conditions will be listed and summarised descriptively by treatment group and study population. A Scatter plot or similar plot will be used to present the individual data by treatment group, and bar chart will be used to present the average paired difference and its standard error.

For the non-inferiority test of words in quiet scores, the 95% CI (alpha=0.025 one-sided) for the mean paired difference will be estimated. If the lower limit of the 95% CI of the mean paired difference is above -10%, the treatment condition is regarded as non-inferior to the control in term of words in quiet perception. The non-inferiority margin of -10% for words in quiet scores (monosyllables) is also based on clinical consensus.

For the non-inferiority test of SRT sentence scores the 95% CI (alpha=0.025 one-sided) for the mean paired difference will be estimated. If the upper limit of the 95% CI of the mean paired difference is lower than 1dB, the treatment condition is regarded as non-inferior to the control in term of SRT sentence perception. The non-inferiority margin of 1dB for SRT is based on clinical consensus.

9.6.2 Secondary Endpoint Analyses

SRT sentence scores in noise and words in quiet scores at different speech testing conditions will be listed and summarised descriptively by treatment group and study population. A Scatter plot or similar plot will be used to present the individual data by treatment group, and bar chart will be used to present the average paired difference and its standard error. Non-inferiority test of words in quiet and SRT sentence scores will be performed as described above in section 9.6.1.

Data from SAR will be summarised descriptively including mean, standard deviation and min/max for quantitative data. Qualitative data will be presented in the appendix of the report and summarised in the results.

9.6.3 Exploratory Endpoint Analyses

SSQ12 and SAR data will be listed and summarised descriptively by treatment group and study population. A Scatter plot or similar plot will be used to present the individual data by treatment group, and bar chart or scatter plot will be used to present the average paired difference and its standard error.

Data from the clinician log and the results for individual questions on the SSQ12 will be summarised descriptively including mean, standard deviation and min/max for quantitative data. Qualitative data will be presented in the appendix of the report and summarised in the results.

9.7 Safety Analyses

For AE, the incidence of occurrence, defined as the proportion of patients who have experienced at least one event, will be reported by intervention group. Similar summaries will be provided for ADEs and DDs. The number and proportion of subjects who died, who discontinued an intervention due to an AE/ADEs, or who experienced a severe or an SAE/SADEs will be summarised separately.

9.8 Interim Analyses

No formal interim analysis will be conducted.

10 INFORMED CONSENT PROCESS

The Investigator shall obtain written informed consent from the subject using an approved ICF prior to any clinical investigation-related examination or activity. The rationale of the clinical investigation, as well as the benefits and risks, what participation will involve, and established alternatives to participation will be explained to the subject in native non-technical language, understandable to the subject. Ample time will be provided for the subject to enquire about details of the clinical investigation and to decide whether to participate.

All questions about the clinical investigation shall be answered to the satisfaction of the subject or the subject's legally acceptable representative. Subjects shall not be coerced or unduly influenced to participate or to continue to participate in a clinical investigation. They shall not waive or appear to waive their legal rights.

Each subject (or their legally designated representative) and the person who conducted the informed consent discussion, shall sign and personally date the Informed Consent Form (ICF). Where required, an independent and impartial witness shall sign and personally date the ICF. A copy of the signed ICF shall be given to the subject. The original signed ICF shall be archived in the Investigator's Site File or subject file at the investigational site.

This process shall be documented in the subject's source documents.

The subject, or the subject's legally designated representative, shall be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the clinical investigation. The communication of this information must be documented as an update to the ICF and re-consent of the subject.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 Definitions

11.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons whether or not related to the medical device or the procedures required for implant or use, and whether anticipated or unanticipated.

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

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

NOTE 3: For users and other persons, this definition is restricted to events related to the use of medical devices.

11.1.2 Adverse Device Effect

An adverse device effect (ADE) is an AE related to the use of a medical device.

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

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

NOTE 3: This includes 'comparator' if the comparator is a medical device.

11.1.3 Serious Adverse Event

A serious adverse event (SAE) is any AE that led to any of the following:

1) death,
2) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:

- a life-threatening illness or injury, or
- a permanent impairment of, or damage to, a body structure or a body function including chronic diseases, or
- in-patient hospitalisation or prolonged hospitalisation, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment or damage to a body structure or a body function,

3) foetal distress, foetal death or a congenital physical or mental abnormality, or birth defect including physical or mental impairment.

NOTE: Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a SAE.

11.1.4 Serious Adverse Device Effect

A serious adverse device effect (SADE) is an ADE that has resulted in any of the consequences characteristic of a SAE.

11.1.5 Unanticipated Serious Adverse Device Effect

An unanticipated serious adverse device effect (USADE) is a SADE, which by its nature, incidence, severity, or outcome has not been identified in the current version of the hazards analysis.

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

11.1.6 Adverse Events of Special Interest

None identified for this clinical investigation.

11.1.7 Device Deficiency

A Device Deficiency (DD) is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

NOTE 1: Device Deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling.

NOTE 2: This definition includes device deficiencies related to the IMD or the comparator.

11.1.8 Serious Health Threat

A signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons.

NOTE: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

11.2 Recording and Handling of Adverse Events

Subjects shall be carefully monitored during the clinical investigation and the investigator should enquire about AEs at investigation visits.

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

Source notes should indicate the evaluation for AEs, even if there was none to report. All required AEs will be reported if observed, even if anticipated and/or acknowledged as a risk factor in the consent.

All AEs will have the following information documented: start and stop dates, action taken, outcome, severity and investigators opinion on the potential relationship to the IMD and/or comparator and study procedures. If an AE changes in severity, the most severe (highest) grade will be captured for that event on the Adverse Events CRF.

11.2.1 Assessment of Severity

The Principal Investigator (or qualified delegate) will make an assessment of severity for each event based on clinical judgement. The intensity of each event recorded in the CRF should be assigned to one of the following categories:

Mild	An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
Moderate	An event that is sufficiently discomforting to interfere with normal activities
Severe	An event which is incapacitating and prevents normal everyday activities

11.2.2 Assessment of Causality

The Investigator will assess the potential causal relationship of each event, using clinical judgement. Alternative causes, such as natural history of underlying diseases, other risk factors and the temporal relationship of the event to the IMD and/or comparator product will be considered and investigated. The causal relationship to the IMD and/or comparator is to be assessed by the Investigator (or medically qualified delegate) and should be assessed using the following classifications:

Not related	Relationship to the medical device or procedures can be excluded when: • the event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has no temporal relationship with the use of the device or the procedures; • the event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; • the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event; • the event involves a body-site or an organ not expected to be affected by the device or procedure; • the event can be attributed to another cause (for example, an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); • the event does not depend on a false result given by the investigational medical device used for diagnosis, when applicable; • harms to the subject are not clearly due to use error; In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.
Unlikely related	The relationship with the use of the medical device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possibly related	The relationship with the use of the medical device is weak but cannot be ruled out completely. Alternative causes are also possible (for example, an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possibly related.
Probably related	The relationship with the use of the medical device seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.
Definitely related	The event is associated with the medical device or with procedures beyond reasonable doubt when: • the event is a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has a temporal relationship with the medical device use/application or procedures; • the event involves a body-site or organ that – the medical device or procedures are applied to

	– the medical device or procedures have an effect on; • the event follows a known response pattern to the medical device (if the response pattern is previously known); • the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible); • other possible causes (for example, an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out; • harm to the subject is due to error in use; • the event depends on a false result given by the medical device used for diagnosis, when applicable; In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.

11.2.3 Assessment of Seriousness

The Investigator will assess the seriousness of each event according to clinical judgement and the definition provided in section 11.1.3.

11.2.4 Assessment of Expectedness

An event should be considered unanticipated if the nature, severity, or frequency of that event is not consistent with the applicable safety reference information, such as the hazards analysis, IB, or Product Information/IFU if the product is approved for marketing.

For this clinical investigation the listed items in Section 8.2 and 8.3 of this CIP are anticipated ADEs.

Anticipated	An adverse device effect (ADE) which by its nature, incidence, severity, or outcome is consistent with the applicable safety reference information (for example, IB, IFU).
Unanticipated	An adverse device effect (ADE) which by its nature, incidence, severity, or outcome is not consistent with, or has not been identified in the applicable safety reference information (for example, IB, IFU).

11.3 Recording and Handling of Device Deficiencies

Subjects shall be carefully monitored during the clinical investigation and routinely questioned about DDs at investigation visits. Source notes should indicate the evaluation for DDs, even if there are none to report.

The Investigator shall assess if the DD led to an AE or could have led to a serious medical occurrence (serious adverse device effect) if;

1. suitable action had not been taken,
2. intervention had not been made, or,
3. circumstances had been less fortunate

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

11.4 Reporting Responsibilities

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

11.4.1 Investigator Reporting of Serious Adverse Events

All AEs meeting the criteria for an SAE, or DD that could have led to an SADE, and AESI, if applicable must be reported to the Sponsor within 24 hours.

Reporting is achieved through completion of the events details in the Adverse Event page of the eCRF.

The Investigator shall always provide an assessment of causality at the time of the initial report, as described in section 11.2.2 'Assessment of Causality'. If data obtained after reporting indicates that the assessment of causality is incorrect, then the SAE form may be appropriately amended, signed, dated, and resubmitted to the Sponsor.

If the Investigator does not have all other information regarding an SAE, he/she will not wait to receive additional information before reporting the event. The reporting forms shall be updated when additional information is received.

The Investigator is responsible for reporting of safety events to their local EC using the applicable report form, in accordance with local regulations.

11.4.2 Sponsor Notification of Events

The Sponsor is responsible for reviewing all safety data to evaluate potential causality and anticipation of all ADEs, and shall conduct an expedited assessment of all SAEs, unanticipated ADEs, DDs that could have led to an SADE, including serious health threat or AESI.

The Sponsor is also responsible for reporting all reportable events according to the requirements and timelines of the regulatory authorities relevant to this clinical investigation. Country specific sponsor reporting responsibilities are outlined in the Sponsor's Safety Data Handling Plan.

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

Name Sponsor Safety Monitor:	Clinical Review Board
Country:	Australia
Phone number:	Not applicable
E-mail:	cltd-safetymonitor@cochlear.com

11.5 Independent Data Monitoring Committee

The risks associated with the use of the investigational device and the subject's participation in the clinical investigation is described in Section 8 of this document. The subjects in the proposed clinical investigation will be able to revert to their own processor if there are sound quality issues or dissatisfaction with the investigational MAPs. As this study is a single-blinded study with regard to the MAPs used for test conditions, no Independent Data Monitoring Committee (IDMC) has been established for this clinical investigation.

12 DEVICE ACCOUNTABILITY

Subjects in the study will be loaned commercially released sound processors that use approved firmware versions. However, these devices will be programmed with dual-electrode mode stimulation mode, using CDI Tool research software which is outside the functionality of the commercial system. As a result, the devices used in this study will follow procedures used for unapproved devices.

Supply of investigational medical devices (loaner study sound processors and CDI Tool software) will be recorded using the Sponsor Device Tracking Form (1295388) and Software Tracking Form (1302326). Investigational medical device(s) software and loaner sound processors will be quarantined at the investigational site and clearly labelled to identify exclusively for use in a clinical investigation.

Subject level device supply will be tracked using the Individual Subject Device Accountability Log Form (1295295). All device(s) that have been identified with Device Deficiencies will be returned to Device Analysis for analysis and archiving. At the end of the clinical investigation, all loaner and unused medical devices shall be returned to the Sponsor.

13 DEVIATIONS FROM THE CLINICAL INVESTIGATION PLAN

The Investigator(s) must not deviate from the CIP, except in case of an emergency to protect the safety and well-being of the subject(s). Such deviations will be documented by the site personnel in the source documentation for the subject and reported to the relevant EC as per institutional requirements and to the Sponsor as soon as possible, but not later than 5 working days from the date of the emergency.

If there is a deviation from CIP-defined assessments or parts thereof are omitted or completed incorrectly, the deviation will also be documented by the site personnel in the source documentation for the subject. Depending on the type or severity of the deviation the Investigator may be required to notify the EC, particularly if the deviation potentially impacts subject safety, performance of IMD and/or comparator, or data integrity.

All CIP deviations will be documented in the eCRF to enable analysis and reporting by the Sponsor in the Clinical Investigation Report (CIR), or to the relevant regulatory authority(s), if applicable.

Gross misconduct on behalf of an Investigator, such as intentional non-compliance with CIP or GCP requirements or fraud, will result in disqualification of the Principal Investigator and/or Investigational Site from participation in the investigation. Data provided by the Principal Investigator or Investigational Site will be excluded from the per-protocol analysis group.

14 DATA MANAGEMENT

The CRF will capture the datapoints necessary to determine the subject status according to the criteria described in section 7.2.5.

14.1 Source Data

Source data will be captured in clinic notes, paper-based source data worksheets, or printed directly from testing software. If electronic medical records do not permit read only access for monitoring purposes, a

certified printout must be provided, indicated by a dated signature by a member of the site team or generated through a validated process.

An Origin of Source Data Form will be used to capture the location of source data kept at each site, outlining the individual site's process for certification.

14.2 Methods for Data Entry and Collection

Data collection will be performed using a commercial electronic data capture (EDC) system on electronic Case Report Forms (eCRFs). Site staff will be trained on the completion of the eCRFs prior to obtaining access to the system and will have their own login/password. Access to clinical study information will be based on an individual's role and responsibilities.

The EDC will use role-based user permissions for data entry, viewing, and reporting options. All communications between users and the EDC server are encrypted. Web servers are protected by a managed firewall. This application is designed to be in compliance with applicable regulations including 21 CFR Part 11.

The application will include programmed data consistency checks and supports manual generation of data clarifications/queries, including documentation of site responses. The application maintains a comprehensive audit trail for all data entered, including updates and queries, and documents the time that each entry occurred and who made the entry.

Principal Investigators will affirm that the data for each subject at their site is accurate and complete by way of an electronic signature.

In addition, de-identified electronically generated data will be collected from clinical fitting software and questionnaires. The unamended data file shall be regarded as the source.

14.3 Database Lock

At the conclusion of the study, the Study Data Manager in consultation with the Clinical Project Manager shall confirm that:

- No further subject visits will be conducted.
- All required forms have been completed in the EDC.
- All required data, including resolution to ongoing Adverse Events in accordance with CIP requirements, have been entered into the EDC.
- All required monitoring, including review of clinical data and Source Document Verification (SDV) according to the Monitoring Plan, has been performed.
- All data queries have been closed.
- All completed eCRFs have been signed by the Principal Investigator or delegate.
- The Statistical Analysis Plan (SAP) is final.
- The Clean File Meeting has been conducted.

15 CONFIDENTIALITY

The investigator and site staff will collect and process personal data of the subjects in accordance with governing data privacy regulations [such as the EU GDPR regulations].

Data will be reported to the Sponsor on CRFs or related documents (for example, questionnaires). Subjects will be identified on CRFs and other related documents only by a unique subject identification code and shall not include the subject's name or other personal identifiable information. Completed CRFs or related documents are confidential and will only be available to the Investigator and site staff, the Sponsor and their representatives, and if requested to the Ethics Committee and national regulatory authorities. Publications or submission to a regulatory authority shall not disclose the identity of any subject.

16 ETHICS COMMITTEE AND REGULATORY AUTHORITY APPROVAL

This clinical investigation will be conducted under a Clinical Trial Notification (CTN) to the Therapeutic Goods Administration.

The clinical investigation will not commence prior to the written favourable opinion or approval from the EC and or regulatory authority (if appropriate) is obtained.

The final Sponsor-approved version of the CIP, Informed Consent Form, and other necessary documents shall be submitted to the EC. A copy of the EC opinion/approval shall be provided to the Sponsor.

The Investigator shall forward to the Sponsor, for review and approval, any amendment made to the approved ICF and any other written information to be provided to the subject prior to submission to the EC.

The Sponsor and Principal Investigator will continue communications with the EC, as required by national regulations, the clinical investigational plan, or the responsible regulatory authority.

Any additional requirements imposed by the EC or regulatory authority will be implemented by the Sponsor.

The Investigator shall submit the appropriate documentation if any extension or renewal of the EC approval is required. In particular, substantial amendments to the CIP, the ICF, or other written information provided to subjects will be approved in writing by the EC.

The Investigator shall report to the EC any new information that may affect the safety of the subjects or the conduct of the clinical investigation. The Investigator will send written status summaries of the investigation to the EC regularly, as per local EC requirements.

Upon completion of the clinical investigation, the Investigator shall provide the EC with a brief report of the outcome of the clinical investigation, as per local EC requirements.

The clinical investigation is covered by clinical trial insurance, meeting the requirements of the participating countries.

17 SUSPENSION OR PREMATURE TERMINATION

The Sponsor will discontinue the clinical investigation site if:

1) major non-adherence to the CIP or GCP principles is occurring

2) it is anticipated that the subject recruitment will not be adequate to meet the objectives of the clinical investigation

An ongoing clinical investigation may be discontinued in case of:

1) device failure

2) serious or intolerable ADE, leading to the explant or discontinued use of the device

3) subject's death

18 AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

No changes in the CIP or investigation procedures shall be made without mutual agreement of the Principal Investigator and the Sponsor. This agreement will be documented as a CIP amendment. Amendments will require notification to the Ethics Committees (ECs) by the Principal Investigators (and to the relevant regulatory authority(s) by the Sponsor, if applicable).

19 RECORD KEEPING AND RETENTION

Data generated from the clinical investigation will be stored in a limited-access file area and be accessible only to representatives of the study site, the Sponsor and its representatives, and relevant health authorities/regulatory agencies. All reports and communications relating to study subjects will identify subjects only by subject unique identification code. Complete subject identification will be maintained by the Investigator. This information will be treated with strict adherence to professional standards of confidentiality.

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

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.

20 PUBLICATION POLICY

This clinical investigation will be prospectively registered on a public clinical trial registry *ClinicalTrials.gov*.

A publication authored by the clinical investigator(s) and Sponsor will be prepared. In addition, the results of the clinical investigation may also be disseminated as conference presentations (for example, abstract and poster session). If a joint peer-reviewed manuscript is deemed appropriate, the authorship and responsibilities will be discussed and agreed upon prior to investigation start and in accordance with guidelines and recommendations provided by the International Committee of Medical Journal Editors (ICMJE)

to enable communication within 12 to 18 months of the Clinical Investigation Report (CIR) approval. All contributors who do not meet the criteria for authorship will be listed in an acknowledgments section of the publication.

21 STATEMENTS OF COMPLIANCE

This clinical investigation shall be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki (World Medical Association, 2013), International Standard ISO 14155:2020 Clinical investigation of medical devices for human subjects - Good Clinical Practice, and any regional or national regulations, as applicable.

22 QUALITY CONTROL AND ASSURANCE

In accordance with Cochlear's Quality Management System, all clinical investigations shall be conducted according to internationally recognised ethical principles for the purposes of obtaining clinical safety and performance data about medical devices.

The Sponsor employees (or designee) shall use standard operating procedures (SOP) to ensure that clinical study procedures and documentation are consistently conducted and compliant with the ISO 14155 Standard, Good Clinical Practice (GCP), and applicable local regulations.

22.1 Monitoring

The Sponsor will perform on-site and remote monitoring visits as frequently as necessary to oversee conduct, data collection and record keeping by sites. The clinical investigation monitoring plan is a separate document for the sponsor to follow, describing all the activities performed during monitoring, and close out.

In accordance with applicable regulations, GCP, and sponsor's/CRO's procedures, monitors will contact the site prior to the start of the study to review with the site staff the CIP, study requirements, and their responsibilities to satisfy regulatory, ethical, and sponsor's requirements. When reviewing data collection procedures, the discussion will also include identification and documentation of source data items.

The sponsor/designee will monitor the site activity to verify that the:

- Data are authentic, accurate and complete
- Safety and rights of subjects are being protected
- Study is conducted in accordance with the currently approved CIP
- Any other study agreements, GCP, and all applicable regulatory requirements are met.

The investigator and the head of the medical institution (where applicable) agrees to allow the monitor direct access to all relevant documents.

22.2 Audits

To ensure compliance with GCP, the CIP, study procedures and applicable regulatory and EC requirements, an independent audit of the study may be conducted. The investigator/institution will be informed of the outcome for audits involving their site.

In addition, inspections by regulatory health authority representatives and EC(s) are possible. An Investigator must, in reasonable time, upon request from a relevant health authority or regulatory agency, permit access to requested records and reports, and copy and verify any records or reports made by the Investigator. Upon notification of a visit by a regulatory authority, the Investigator will contact the Sponsor immediately.

The Investigator will grant the Sponsor representatives the same access privileges offered to relevant health authority or regulatory agents, officers, and employees, for the purposes of a Sponsor audit of the site, or in preparation for an inspection.

Audits and inspections may occur at any time during or after completion of the study.

23 TRADEMARKS AND COPYRIGHT

24 REFERENCES

24.1 Internal references

Document Title	Number
Clinical investigation report CRC5523 Clinical Evaluation of Dual Electrode Mode	557516
Cochlear Quality Manual reference	1141823
Device Tracking Form	1295388
Nucleus 7 sound processor user guide	D815387
Nucleus 8 sound processor user guide	D2142802
Individual Subject Device Accountability Log Form	1295295
Kanso 2 sound processor user guide	D1608850
Software Tracking Form	1302326

24.2 External references

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World Medical Association. (2013). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*, *310*(20), 2191–2194. https://doi.org/10.1001/jama.2013.281053

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25 CHANGE HISTORY

Version	Change	Rationale
1	Initial Release	NA
	In section 14.2 the boiler plate text has been changed to remove reference to Medidata Rave EDC	This study will not use Medidata Rave EDC as Cochlear is transitioning to a new EDC system.
	In section 20 the boiler plate text has been updated.	To reflect current requirements and timelines.

26 APPENDIX 1: SWITCHING ACCEPTABILITY RATING

The SAR is designed to measure the sound quality differences between two programs and assess the difficulty in acclimating to a new program after listening to it for 10 minutes.

Question 1 is to be answered soon after switching to a different program.

1) How does the sound quality of the new program compare with the earlier program in terms of sound quality?
    1. Very different
    2. Somewhat different
    3. Similar
    4. Same

Question 2 is to be answered after the subject had an opportunity to listen with the different program for a minimum of 10 minutes.

2) How difficult was it to get used to the new program after listening to it for 10 minutes?
    1. Very Difficult
    2. Difficult
    3. Neutral
    4. Easy
    5. Very Easy

Additional comments

_____

_____

_____

_____

_____

_____

27 APPENDIX 2: CLINICIAN LOG

No.	Date	Condition	Clinician action	Patient response
1	*01/01/2024*	*LP3*	*Went live with default MAP converted to DE mode*	*All sounds too loud*
2	*01/01/2024*	*LP3*	*Reduced all C levels by 2 CL*	*Still too loud*
3	*01/01/2024*	*LP3*	*Reduced all C levels by 2 CL*	*Sound is comfortable*
4				
5				
6				
7				

(Grey text indicates examples of log entries)