Clinical Investigation Plan

Investigation Title: A Pre-Marketing, Prospective, Single-Site, Open-Label, Within-Subject, Pivotal, Interventional Study of Acceptance and Performance with experienced adult cochlear implant recipients using the CP1110 Sound Processor compared with the CP1000 Sound Processor

Short Title:	**PINNA Study**
CIP Number:	**CLTD5810**
Date:	***Refer to header***
Sponsor	**Cochlear Limited**
	1 University Ave
	Macquarie University, NSW, 2109
	[redacted]

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

ClinicalTrials.gov ID:NCT05080283

Manufacturer	Cochlear Limited 1 University Ave Macquarie University, NSW, 2109
Investigator	[redacted] Principal Research Audiologist Cochlear Limited 1 University Ave Macquarie University, NSW, 2109
Safety Contact	[redacted]

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.

Name	**Title**
[redacted]	Principal Investigator
Signature	**Date**

TABLE OF CONTENTS

1 DEFINITIONS AND ABBREVIATIONS

Term	Description
ADE	Adverse Device Effect
AE	Adverse Event
AMDT	Approved Medical Device on Test
BEAM	Adaptive beamformer – Microphone directionality
BTE	Behind the ear
CDI	Cochlear Device Interface
CER	Clinical Evaluation Report
CI	Cochlear Implant
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CNC	Consonant nucleus consonant
COSI	Client Orientated Scale of Improvement
CRF	Case Report Form
CRO	Contract Research Organisation
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
FF	ForwardFocus
EDC	Electronic Data Capture
GCP	Good Clinical Practices
GT	Gain threshold. For Noise reduction algorithms.
IB	Investigator's Brochure
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
IMD	Investigational Medical Device
N7	Nucleus 7 System
N8	Nucleus 8 System
NCA	National Competent Authority

Term	Description
OTE	Off the ear
PI	Principal Investigator
PIL	Principal Investigator List
PMS	Post-Market Surveillance
QoL	Quality of Life
S0N0	Signal and noise from 0 degrees azimuth
S0N90	Signal from 0 degrees and noise from 90 degrees azimuth
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCAN	Automatic Scene Classifier
SNR-NR	Signal to noise ration noise reduction
SOP	Standard Operating Procedure
SP	Sound Processor
SSQ	Speech Spatial and Qualities of Hearing Scale
SRT	Speech Recognition Threshold
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
Zoom	Fixed directional beamformer

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A Pre-Marketing, Prospective, Single-Site, Open-Label, Within-Subject, Pivotal, Interventional Study of Acceptance and Performance with experienced adult cochlear implant recipients using the CP1110 Sound Processor compared with the CP1000 Sound Processor
Short title	PINNA Study
Investigation number	CLTD5810
Name of investigational medical device(s)	Nucleus 8 Sound Processor including: CP1110 Processing Unit CP1110 Sound Processor Firmware CP1110 Slimline Coil Custom Sound (Version 7.0) Nucleus Smart App 6.0
Intended use of investigational medical device(s)	The Nucleus 8 Sound Processor (Model: CP1110) is an unapproved investigational medical device. The intended use for the Nucleus 8 Sound Processor will be the same as for the approved Nucleus 7 Sound Processor: The Nucleus 7 Series Processing Units are intended to be used in combination with other devices as part of a hearing implant system to provide hearing sensation. The processing unit converts sounds into electrical signals, which it sends, via a coil, to an implant. The processing unit also provides power to the implant. When used in combination with an acoustic receiver, the sound processor also delivers sound to the ear canal in recipients with residual hearing[1]
Name and description of comparator device/product(s)	The Nucleus 7 Processing Unit (Model CP1000) is approved for use in Australia.
Estimated recruitment period	2 months
Expected duration per subject	12 months
Number of subjects planned	20
Number of investigational sites planned	1
Inclusion criteria	1) Aged 18 years or older 2) Post lingually deafened 3) Implanted with the CI600 Series (CI612, CI632, CI622, CI624), CI500 Series (CI512, CI532, CI522) or Freedom Series (CI24RE(CA), CI24RE(ST), CI422)

[1] The acoustic receiver will not be available for this study

	4) At least 6 months experience with a cochlear implant. 5) At least 3 months experience with a Nucleus 7 (CP1000) Sound Processor 6) Able to score 30% or more at +15 SNR with CI alone on a sentence in babble test 7) Willingness to participate in and to comply with all requirements of the protocol. 8) Fluent speaker in English as determined by the investigator 9) Willing and able to provide written informed consent
Exclusion criteria	1) Additional disabilities that would prevent participation in evaluations. 2) Unrealistic expectations on the part of the subject, regarding the possible benefits, risks and limitations that are inherent to the procedures. 3) Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator. 4) Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling. 5) Cochlear employees or employees of Contract Research Organisations or contractors engaged by Cochlear for the purposes of this investigation. 6) Currently participating, or participated in another interventional clinical study/trial in the past 30 days or if less than 30 days, the prior investigation was Cochlear sponsored and determined by the investigator to not impact clinical findings of this investigation.

Objectives and Endpoints	
Primary Objective	**Primary Endpoint**
To evaluate adult cochlear implant speech perception in spatially separated speech and noise (S0Nrearhalf) with the CP1110 Sound Processor with ForwardFocus ON (SCAN) compared with ForwardFocus OFF (SCAN)	Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus ON (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0Nrearhalf 4TB).
Secondary Objective	**Secondary Endpoint**
To evaluate adult cochlear implant speech perception in spatially separated speech and noise (S0N3) with the CP1110 Sound Processor with ForwardFocus ON (SCAN) compared with ForwardFocus OFF (SCAN)	Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus On (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0N3 Babble).

To evaluate adult cochlear implant speech perception in quiet with the CP1110 Sound Processor and the Nucleus 7 Sound Processor	Paired difference in percentage CNC Words correct in quiet (50 dB) with the CP1110 Sound Processor and Nucleus 7 Sound Processor
To evaluate adult cochlear implant subjective hearing performance and sound quality with the CP1110 Sound Processor and Nucleus 7 Sound Processor	Paired difference in Global SSQ12 scores after experience with the CP1110 Sound Processor and Nucleus 7 Sound Processor
To evaluate acceptance and satisfaction of the CP1110 Sound Processor	Ratings on the 'CP1110 Questionnaire 1' and 'CP1110 Questionnaire 2' after at least 2 weeks of experience with the CP1110 Sound Processor
Exploratory Objective	**Exploratory Endpoint**
To evaluate the ease of use and user experience of the CP1110 Sound Processor System when used in real world conditions	Take home use with the CP1110 Sound Processor System

3 SCHEDULE OF EVENTS

Visit Type	Screening	Visit 1[a]	Visit 2	Visit 3	Visit 4	Additional visit[b]	Visit 5
Written informed consent	X						
Demographics	X						
Eligibility	X						
Hearing history	X						
Device history	X						
Medical history	X						
Sound Quality Assessment		X[b]	X[b]	X[b]	X[b]		X[b]
Usability Assessment		X	X	X[b]	X[b]		X[b]
Fit and optimise Nucleus 8 Device		X	X	X	X	X	X
Speech perception testing – S0Nrearhalf						X	
Speech perception testing – S0N3						X	
Speech perception testing – Words in Quiet						X	
Baseline Survey		X					
CP1110 Questionnaire 1			X				
CP1110 Questionnaire 2					X		

Visit Type	Screening	Visit 1[a]	Visit 2	Visit 3	Visit 4	Additional visit[b]	Visit 5
SSQ12 – Nucleus 7		X					
SSQ12 – Nucleus 8			X				
Concomitant medications/therapies	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X
Device Deficiencies		X	X	X	X	X	X
Device exposure		X	X	X	X	X	X

Abbreviations: CI, cochlear implant; QoL, quality of life; EOS, End of Study

[a] Screening and visit 1 may occur on the same day for subjects.

[b] Optional test.

See section 7.3 for more details on the adaptive procedure that will be implemented if certain product issues are identified

Visits may be in-clinic or remote. See section 7.3.7 for the Covid-19 related provisions that may be utilised of restrictions are in place during the study period.

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

This clinical study aims to investigate acceptance, actual-use usability and speech performance with the new Nucleus 8 Sound Processor (model: CP1110) system, compared with the commercially available Nucleus 7 Sound Processor (model: CP1000) system, with particular focus on the acceptance of and satisfaction with the noise reduction feature ForwardFocus in the Automatic Scene Classifier 'SCAN'.

This study will build on the evidence collected in previous Nucleus 7 Sound Processor take home studies (see section 4.2.2), and will also aim to confirm the in-booth performance of Nucleus 8 and Nucleus 7 Sound Processors.

In this document, Nucleus 7 Sound Processor will be abbreviated to Nucleus 7 SP and will always refer to the sound processing unit model name CP1000, and Nucleus 8 Sound Processor will be abbreviated to Nucleus 8 SP and will always refer to the sound processing unit model name CP1110.

4.2 Findings of Previous Nonclinical and Clinical Studies

4.2.1 Nonclinical Data

Biological safety evaluation of the Nucleus 8 SP and accessories was conducted in compliance with:

- ISO / EN ISO 10993-1:October 2009 Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process
- EN45502-2-3:2010 Active implantable medical devices Part 2-3: Particular requirements for cochlear and auditory brainstem implant systems

Testing has confirmed that materials of the Nucleus 8 SP and accessories that are in contact with skin are biologically safe and suitable for use.

4.2.2 Clinical Data

Clinical data relevant for the current trial fall under two main categories 1) Evidence on previous Behind the Ear (BTE) SP generations and 2) Evidence on the development and approval of ForwardFocus. These clinical data are summarized below:

Behind the Ear Clinical Data

Most clinical evidence on the previously marketed BTE SP, Nucleus 7 SP is available from two Cochlear-sponsored clinical studies that have been carried out in Australia. These studies included some assessments very similar to those planned in the present study. These Cochlear sponsored studies and reports from published literature are summarized below:

Clinical Evaluation of Nucleus 7 Cochlear Implant System (CLTD5620)

The in-house study aimed to collect subjective impressions of the Nucleus 7 SP and associated accessories (CR310 and Nucleus Smart App) and to evaluate speech recognition performance of the Nucleus 7 SP in quiet and noise. A total of 46 subjects were enrolled in the study.

The Client Orientated Scale of Improvement (COSI) indicated a greater proportion of “benefit” vs. “no benefit” in eight of the nine categories covered by the responses. An additional custom questionnaire was devised to assess listening benefits provided by the CI system for specific aspects of hearing. Mean scores favoured the Nucleus 7 SP for all 27 questions, with significant differences for 11 questions. Cochlear implant specific quality of life (QoL) was measured via the Nijmegen questionnaire and for all three sub-domains (physical, psychological and social) there were significant improvements in QoL change greater than that expected by chance.

Mean speech recognition scores in quiet (CNC monosyllables) were not significantly different among the Nucleus 5, Nucleus 6, and Nucleus 7 SPs. The results of the adaptive sentences in noise test in the S_0N_0 condition showed that the mean speech recognition performance in noise with both the Nucleus 7 SP (SCAN) and Nucleus 6 SP (SCAN) was significantly better than with the Nucleus 5 SP (Zoom). In spatially separated noise, there were statistically significant performance differences between the Nucleus 5 SP (Zoom) and Nucleus 7 SP (SCAN). Overall, the speech recognition outcomes demonstrated equivalent performance for the Nucleus 7 SP (SCAN) and Nucleus 6 SP (SCAN) in both quiet and noisy test conditions.

The use of the Cochlear MiniMic 2+ and Phonak Roger 20 wireless microphones was compared with the Nucleus 7 SP SCAN baseline. Sentence recognition scores in both microphone conditions were significantly better than baseline. Performance with the MiniMic 2+ was significantly better than performance with the Roger 20 when speech was presented in noise.

Results of this study have been published(Warren, Nel, & Boyd, 2019).

ForwardFocus Clinical Data

Signal processing strategies are designed to remove some or all competing noise, while maintaining the target speech with little or no modification. The SNR-NR algorithm that was introduced in CP910/920 uses a single microphone or single channel input, is non-directional and performs best in steady-state background noise. The performance benefit is reduced in more modulated (non-stationary) noise such as when there are competing talkers (Dawson et al., 2011; Hersbach et al., 2012).

In contrast, ForwardFocus uses two fixed-directional microphones to capture spatial information, enabling noise to be filtered based on the location of the sound source. The signal of interest is defined as originating from in front of the listener and noise as originating behind or to the sides of the listener. If SNR-NR is enabled, it can operate on the output signal from ForwardFocus. The two noise reduction algorithms complement each other due to their different principles of operation. Hersbach et al. (2013) found that ForwardFocus provided a significant improvement in group mean speech reception threshold compared with BEAM.

A clinical evaluation of ForwardFocus performance (CRC5513), using the Nucleus 6 Sound Processor (Model CP910), revealed higher group mean speech perception scores with ForwardFocus (Zoom+Strong) than with Standard, Zoom or Beam(Z) (a modification of Beam that uses Zoom directionality) when speech was presented from the front of the listener and noise presented from the rear. Higher group mean speech recognition scores were also obtained with ForwardFocus compared to Standard and Zoom algorithms with speech presented from the front of the listener and speech weighted noise (SWN) from the rear. Group mean ratings for sound quality ratings were higher with ForwardFocus than with Standard, Zoom or Beam(Z). There was no

significant group difference in SSQ rating between ForwardFocus and the comparator programs (Standard, Zoom or Beam(Z)). There was an overall preference for “SCAN” with ForwardFocus over “SCAN” alone. The investigators concluded that ForwardFocus is most useful at improving speech intelligibility when the competing sources are to the sides and/or rear of the listener.

In study CRC5589/CTC5614, using the Nucleus 6 Sound Processor (Model CP910), speech perception outcomes and acceptance for three different strengths of ForwardFocus integrated with SCAN were compared with SCAN plus SNR-NR (N6 SCAN). Sentence recognition scores with noise in rear half noise was significantly better with all ForwardFocus programs than N6 SCAN. Word recognition scores in quiet and questionnaire ratings for all ForwardFocus programs were comparable to N6 SCAN. Sentence-in-noise scores obtained with speech and noise presented from the front were non-inferior to N6 SCAN for mild ForwardFocus only. A decrement compared with ForwardFocus Strong was found. Sentence in noise scores with speech presented to the cochlear implant side or from behind the listener with mild ForwardFocus were inferior to the baseline. Based on these findings the investigators recommended that ForwardFocus be introduced as a custom programme that could be selected for specific listening conditions.

Study CLTD5606 was designed to assess the effectiveness of ForwardFocus for speech reception in noise compared with the Nucleus 6 SCAN (SCAN + SNR-NR). The study included twenty-five conventional CI recipients. For sentence recognition with four-talker babble from the rear, all three levels of ForwardFocus (strong, medium and mild) were found to be superior to the Nucleus 6 SCAN. For speech-weighted noise presented behind the listener ForwardFocus Strong was demonstrated to be superior to the Nucleus 6 SCAN. When speech and either speech-weighted noise or four-taker babble were co-located in front of the listener, sentence recognition with ForwardFocus strong was similar to the Nucleus 6 SCAN. For CNC words in quiet ForwardFocus Strong was inferior to the Nucleus 6 SCAN. The investigators concluded that acceptable performance and safety of the ForwardFocus program can be anticipated for Nucleus 7 SP users in noisy environments, and the risk versus benefit profile is acceptable when ForwardFocus be used in quiet environments.

The in-house study CLTD5709 investigated the effect of ForwardFocus noise reduction on adult cochlear implant recipients’ speech perception scores, listening effort and subjective ratings using the Nucleus 7 SP. A total of 24 subjects were enrolled in the study.

Speech perception with babble noise from the rear demonstrated that ForwardFocus On was superior to ForwardFocus Off (Nucleus 7 default program SCAN). Listening effort as measured via a dual-task paradigm involving both speech perception and a visual reaction time task revealed no significant difference in reaction times between ForwardFocus On and ForwardFocus Off, and therefore no difference in listening effort.

Questions from the Speech domain of the ‘Speech, Spatial and Qualities of Hearing Scale’ (SSQ) and 3 questions from the Qualities of Hearing domain were completed by subjects at baseline and after at least 4 weeks of use with ForwardFocus. The mean Speech domain results collected after 4 weeks of use were not significantly different from baseline scores.

Subjective ratings on the custom questionnaires indicated strong satisfaction, ease of use, and confidence with ForwardFocus. The majority of respondents found the ForwardFocus controls within the Nucleus Smart App as very easy to use and half of the respondents wanted ForwardFocus on their own processor.

4.3 Study Rationale

This investigation is planned to investigate the performance and clinical benefits of features that are new to the Nucleus 8 Sound Processor compared with the predicate device, the Nucleus 7 Sound Processor. This study will build on the evidence previously collected on BTE sound processors and 'ForwardFocus', with particular focus on the acceptance and satisfaction of the automation of ForwardFocus, and the sound processor system in general.

The key indicators of clinical performance and benefit include:

- AuSTIN Sentences in noise (hearing performance)
- Monosyllabic words in quiet (hearing performance)
- The subjective Speech and Spatial Qualities scores (as available)

A more detailed description of the test conditions and rationale for their inclusion is available in Table 2.

5 MEDICAL DEVICE INFORMATION

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

Nucleus 8 Sound Processor (CP1110)

The Nucleus 8 SP is a Behind-The-Ear sound processor to be used with a compatible Cochlear Implant and is manufactured by Cochlear Limited. The Nucleus 8 SP is an incremental refinement of the Nucleus 7 SP, and re-uses many of the existing technology and features of the Nucleus 7 SP.

The minimum components required for normal operation of the Nucleus 8 SP are:

- CP1110 processing unit
- CP1110 Slimline coil,
- CP1110 Rechargeable Battery module
- CP1000 Magnets (approved devices)
- CP1110 Earhooks

The Nucleus 8 SP incorporates the NEO-XS processor chip and C6 Hybrid chip, which allows for a smaller size sound processor, improved audio processing and improved support for GN ReSound Accessories when compared to previously marketed devices.

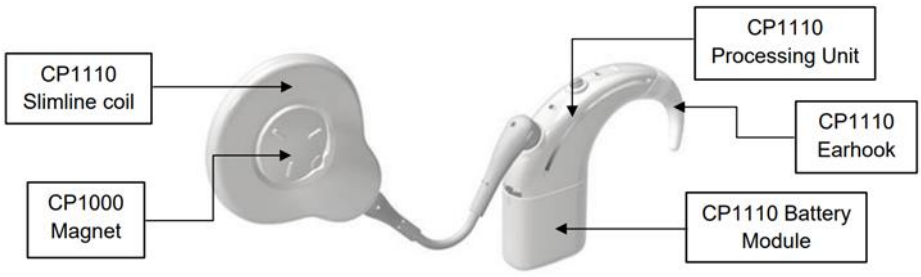

Figure 1: Image of the Nucleus 8 SP

The key component similarities compared with the previous generation (Nucleus 7) include swappable rechargeable or 2ZincAir batteries, an integrated coil and coil cable, a single push button, manual selection of ForwardFocus which is an algorithm that reduces noise from behind and beside the listener while passing sounds from the front without attenuation. The product features intended for commercialisation also include three different receiver sizes for hybrid support, compatibility with True Wireless accessories, GN Resound hearing aids to enable bimodal operation.

The Nucleus 8 SP includes access to sound processor controls via the CR310 Remote Control and the Nucleus Smart App on compatible iOS and Android Phones. The Nucleus 8 Sound Processor will be programmable using Custom Sound Pro fitting software.

The key component differences compared with the previous generation (Nucleus 7) include Bluetooth 5.2 Hearing Aid Profile (BTHAP) capable hardware (C6 Hybrid), and reduced size [redacted]. The Nucleus 8 SP also includes access to low energy audio streaming from mobile phones and BTHAP broadcasts and compatibility with next generation Cochlear [redacted] Implants.

Additional features introduced in the sound processor include improved accuracy of the SCAN algorithm (SCAN-X), automation of ForwardFocus in SCAN-X, [redacted]

SCAN-X is a development of the SCAN automation system. Like SCAN, it switches directional processing modes based on an environmental classifier, that predicts whether the recipient is in a Quiet, Speech, Speech in Noise, Noise or Music environment from the microphone signal. The underlying environmental classifier in SCAN-X does additional analysis on the spectrum of the signal to improve its prediction accuracy.

The new adaptive ForwardFocus in SCAN-X feature (SCAN+FF) will apply the ForwardFocus noise attenuation processing algorithm using different strengths in conjunction with the microphone directionality modes already used in SCAN (namely Standard, Zoom, and Beam directionality modes).

The additional features and upgrades in technology of the Nucleus 8 Sound Processor are anticipated to improve the usability, hearing performance and aesthetics of the device in comparison to currently marketed devices.

Processing Unit

The main functions of the Nucleus 8 Sound Processor are executed by the CP1110 Processing Unit. The CP1110 Processing Unit houses the electronics and processing unit firmware necessary for the sound processor to function and provides the interfaces for other devices and accessories. The CP1110 Processing Unit will be available in six colours and is supplied with the Cochlear Earhook (medium).

The CP1110 Processing Unit will be commercially called Nucleus® 8 Processing Unit. The CP1110 Processing Unit consists of a printed circuit board assembly (PCBA) held together in a PCBA skeleton which is encapsulated by the top cover and the processor case. The [redacted] microphones are protected by the microphone cover sitting on top of the top cover. The processor case is closed with a Cochlear proprietary NEUF connector which is used to connect to the battery module or other accessories.

- The materials in contact with skin are:
    - Processing unit casing: Co-polyester Tritan MX731
    - Earhook (hard part): Polyamide Grilamid TR90 Clear
    - Earhook (soft part): Silicone ShinEtsu KE 2090/70

Nucleus 8 Coils

The Nucleus 8 coils will be based on the Nucleus 7 coils design. The mechanical shells of the coils are identical between the Nucleus 7 and Nucleus 8 coils, but the Nucleus 8 coils incorporate a new coil connecter and coil printed circuit boards (PCBs). The materials in contact with skin include:

- Coil overmould and strain relief overmould: TPE 27A70
- Coil cable sheath: Totoku PVC

Magnets

Nucleus 8 Sound Processor will use the same magnets as the Nucleus 7 Sound Processor. The materials in contact with skin are:

- Magnet casing: ABS Colorcomp HMG94MDC

Battery Modules

The CP1110 Processing Unit in stand-alone mode can be powered by three different battery options:

- Compact Rechargeable battery (91mAh)
- Power compact Rechargeable battery (142mAh)
- Power Extend Rechargeable battery (183 mAh)

The materials in contact with skin include:

- Battery casing: Co-polyester Tritan MX731

Intended Use

The Nucleus 8 Processing Units are intended to be used in combination with other devices as part of a hearing implant system to provide hearing sensation. The processing unit converts sounds into electrical signals, which it sends, via a coil, to an implant. The processing unit also provides power to the implant.

When used in combination with an audio receiver, the sound processor also delivers sound to the ear canal in recipients with residual hearing.

The IMD and/or the packaging for the device will state that the device is exclusively for use in a clinical investigation.

Intended Population

The SP is indicated for a recipient with a compatible Cochlear Nucleus implant. The SP is compatible with the following Cochlear Nucleus implants:

- CI600 Series Implants: CI612, CI622, CI624, CI632
- CI500 Series Implants: CI512, CI522, CI532, ABI541
- CI24RE Series Implants: CI422, CI24REH (Hybrid L24), CI24RE (CA), CI24RE (ST)
- CI24R and CI24M Series Implants: CI24R (CA), CI24R (CS), CI24R (ST), CI24M, ABI24M, CI11+11+2M

All medical devices used in this investigation are manufactured by Cochlear Limited.

5.2 Identity and Description of the Comparator

Nucleus 7 Sound Processor (CP1000)

Nucleus 7 is a sound processor system manufactured by Cochlear Limited. The Nucleus 7 SP is commercially available. The sound processor is controlled by either the Nucleus Smart App (on iOS or Android), the MFi Control (on the iPhone, iPad or iPod Touch), the Remote Control (CR310) or the button on the sound processor. Recipients can monitor the sound processor using the Android or iPhone Nucleus Smart App. Clinicians can program the Nucleus 7 SP with Custom Sound Pro (6 or later).

The Nucleus 7 SP incorporates the NEO-XS processor chip, which allows for a small sound processor, low power usage, improved audio processing and improved support for GN ReSound Accessories when compared to the previous CP910/CP920 Sound Processors.

Figure 2: Image of the Nucleus 7 SP (Model: CP1000)

The key component differences compared with the previous generation (Nucleus 6) include an integrated coil and coil cable, a single push button instead of two buttons used in the N6 sound processor, three different receiver sizes for hybrid support, compatibility with GN Resound hearing aids to enable bimodal operation via MFi, the introduction of ForwardFocus, and access to sound processor controls via the Nucleus Smart App on compatible Apple and Android Phones.

Table 1 Nucleus 7 and Nucleus 8 SP Feature Comparison. Asterisks (*) denote features that will not be available with the Nucleus 8 SP for the trial.

Product Name	**Nucleus 7 SP**	**Nucleus 8 SP**
Model Number	**CP1000**	**CP1110**
		
[redacted]		
Dimensions (Processing unit+Standard Rechargeable Battery+medium earhook) **volume** **length** **height**	6.5 cm^3 44.98 mm 43.11 mm	6.0 cm^3 41.9 mm 43 mm
Weight	10.16 g (with 2ZnAir batteries) 9.83 g (with Standard Rechargeable battery) 7.95 g (with Compact Rechargeable battery)	9.5g (with 2ZnAir module)* 9.5g (with Power Extend Rechargeable battery) [redacted] 7.0g (with Compact Rechargeable battery)*
Colour range	5 colours and 2 detail options	6*
Direct Streaming Choice	Android iPhone	Android iPhone

	Telecoil	Telecoil Bluetooth 5.2 Hearing Aid Profile*
Wireless Accessory support	Prox 2	Prox 2
Input Processing Technologies	ADRO ASC Whisper Standard Zoom BEAM SNR-NR WNR FF Manual SCAN	ADRO ASC Whisper Standard Zoom BEAM SNR-NR WNR FF Manual SCAN+FF SCAN X
Core Control: CR310, Nucleus Smart App.		
Core Connected Care: Remote Check*-ready, CS Pro programming software		

Table 2 Outcome measure comparisons and rationale

Test condition	Comparison	Rationale
Sentences in noise S0Nrearhalf babble (65 dB SPL)	Treatment: Nucleus 8 SCAN+FF Control: Nucleus 8 SCAN	ForwardFocus is designed to reduce sounds that originate from behind the listener. The inclusion of S0Nrearhalf and S0N3 speaker configurations, with the noise originating from behind, will facilitate confirmatory testing of SCAN+FF compared with the default SCAN configuration while controlling for the sound processor hardware including new microphones, and the new underlying scene classifier. This will be the first evaluation of SCAN+FF using a more disparate and variable noise type (S0Nrearhalf) and fixed-speaker noise (S0N3), and will provide an indication of the performance of ForwardFocus Auto in a variety of noise positions.
Sentences in noise S0N3 babble (65 dB SPL)	Treatment: Nucleus 8 SCAN+FF Control: Nucleus 8 SCAN	
CNC words in Quiet (50 dB SPL)	Treatment: Nucleus 8 standard directionality Control: Nucleus 7 standard directionality	[redacted]
SSQ12	Treatment: Nucleus 8 Sound Processor Control: Nucleus 7 Sound Processor	The SSQ includes a variety of hearing situations that reflect the reality hearing in the everyday world. The inclusion of this measure, coupled alongside the in-booth testing, allows for a complete picture of benefit associated with the signal processing technology. Study subjects will be asked to complete the SSQ12 at two time points in the study; 1) at study entry, where scores will reflect their experience with their own sound processor, 2) after take home use with the Nucleus 8 Sound Processor.

6 OBJECTIVES

6.1 Primary Objective

To evaluate adult cochlear implant speech perception in spatially separated speech and noise (S0Nrearhalf) with the CP1110 Sound Processor with ForwardFocus ON (SCAN) compared with ForwardFocus OFF (SCAN)

6.2 Secondary Objective

- To evaluate adult cochlear implant speech perception in spatially separated speech and noise (S0N3) with the CP1110 Sound Processor with ForwardFocus ON (SCAN) compared with ForwardFocus OFF (SCAN)
- To evaluate adult cochlear implant speech perception in quiet with the CP1110 Sound Processor and the Nucleus 7 Sound Processor
- To evaluate adult cochlear implant subjective hearing performance and sound quality with the CP1110 Sound Processor and Nucleus 7 Sound Processor
- To evaluate acceptance and satisfaction of the CP1110 Sound Processor

6.3 Exploratory Objective

To evaluate the ease of use and user experience of the CP1110 Sound Processor System when used in real world conditions

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

This is a pre-market, prospective, single-site, non-randomised, open-label, within-subject, pivotal, interventional clinical investigation.

The subjects include adults aged 18 years and older with sensorineural hearing impairment who are current users of a Nucleus Cochlear Implant system and Nucleus 7 Sound processor system. After enrolment, subjects will attend scheduled study visits over a twelve month study period as described in the CIP Schedule of Events (Section 3). At study visits, subjects will undergo hearing assessments. 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

Experienced adult cochlear implant recipients have been chosen as the study population due to their ability to compare sound processors across generations, in and outside of the booth. In addition, performance benefits achieved by adults can generally be extrapolated to younger age groups, avoiding the need to recruit this vulnerable population.

Comparison will be made within-subject with repeated measures for each of the sound processing conditions to be evaluated. There will be at least 5 in-clinic sessions with take home use between each sessions. The test sessions will include speech perception tests including sentence in noise and words in quiet tests and may include the completion of questionnaires and usability assessment. These speech measures are routine outcome measures used to evaluate new signal processing algorithms and hardware.

There will be no blinding of the study investigators.

Blinding of the study subject will be undertaken where possible, particularly when multiple signal processing conditions are loaded onto a single study device. Patients will not be told which program will be used in which order, and due to the similar form factor of the SP generations, it may also be possible to conceal which SP is being used during testing.

Counter-balancing 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 or subject's legally authorised representative before any study procedures are initiated.

To maintain confidentiality, subject names will not be recorded on any study document other than the informed consent form and Subject ID Log; neither document will be provided to the Sponsor. All individuals who provide informed consent are considered enrolled into the study and will be assigned a unique identifier. If a subject signs consent and either exits the study or fails the screening assessments prior to initiating Visit 1, they will be considered a screen failure and will not be counted as part of the required 20 subjects for the study.

The subjects include men and women aged 18 years or older with at least 3 months experience with a Nucleus 7 (CP1000) Sound Processor system. Subjects will be screened, and 20 eligible subjects will be recruited in the clinical investigation. For speech perception testing, all subjects will receive all treatment and control conditions; however, the test order will be counterbalanced/ randomised to control for order effects.

7.2.1 Inclusion Criteria

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

1) Aged 18 years or older
2) Post lingually deafened
3) Implanted with the CI600 Series (CI612, CI632, CI622, CI624), CI500 Series (CI512, CI532, CI522) or Freedom Series (CI24RE(CA), CI24RE(ST), CI422)
4) At least 6 months experience with a cochlear implant.
5) At least 3 months experience with a Nucleus 7 (CP1000) Sound Processor
6) Able to score 30% or more at +15 SNR with CI alone on a sentence in babble test
7) Willingness to participate in and to comply with all requirements of the protocol.

8) Fluent speaker in English as determined by the investigator

9) 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) Additional disabilities that would prevent participation in evaluations.
2) Unrealistic expectations on the part of the subject, regarding the possible benefits, risks and limitations that are inherent to the procedures.
3) Unable or unwilling to comply with the requirements of the clinical investigation as determined by the Investigator.
4) Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.
5) Cochlear employees or employees of Contract Research Organisations or contractors engaged by Cochlear for the purposes of this investigation.
6) Currently participating,or participated in another interventional clinical study/trial in the past 30 days or if less than 30 days, the prior investigation was Cochlear sponsored and determined by the investigator to not impact clinical findings of this investigation.

7.2.3 Number of Subjects Required

See Section 9.4 Sample size considerations

7.2.4 Vulnerable Populations

Pregnant women will not be excluded from this study. The study procedures including the investigational devices will have no impact on the health and safety of this population.

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 prior to initiating Visit 1.
- Participated: Subjects who have met eligibility criteria and have commenced baseline assessments.
- Withdrawn: An Enrolled subject who withdrew or was withdrawn by the Investigator or Sponsor before the expected End of Study visit. Withdrawn subjects may still continue in safety follow up until their scheduled End of Study visit, for reasons described in section 7.2.6.
- Completed: Enrolled subjects who have completed the required treatment and visit schedule.

The recruitment period for the clinical investigation is estimated to be 2 months from the time of first subject consent to recruitment of the last subject.

The expected duration of each subject's participation in the clinical investigation, is up to 12 months from the time of informed consent through to the last study visit.

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 for Subject Withdrawal

Subjects can decide to withdraw from the investigation at any time and are not obliged to provide any justification for their decision. The Investigator shall ask the reason(s). The reason for withdrawal should be documented in the subject's source files and the case report form (CRF).

The Investigator or Sponsor may also decide to withdraw a subject from the clinical investigation 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

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 will not be replaced.

7.2.7 Randomisation Procedures

Subjects will not be randomised to a treatment condition. To control for order effects, counterbalancing of the test order will be implemented for the primary and secondary speech perception endpoints. All permutations will be represented evenly across the subjects where possible.

SRT S0Nrearhalf Test order

Primary: Nucleus 8 (SCAN+FF) vs Nucleus 8 (SCAN)

Subjects assigned a study ID including ODD numbers (01, 03, 05 etc) will be tested in the following order:

1. Nucleus 8 (SCAN+FF)
2. Nucleus 8 (SCAN)

SRT S0N3 Test order

Secondary: Nucleus 8 (SCAN+FF) vs Nucleus 8 (SCAN)

Subjects assigned a study ID including EVEN numbers (02, 04, 06 etc) will be tested in the following order:

1. Nucleus 8 (SCAN+FF)
2. Nucleus 8 (SCAN)

CNC Words Test Order

Secondary: Nucleus 8 vs Nucleus 7

Subjects assigned a study ID including ODD numbers (01, 03, 05 etc) will be tested in the following order:

1. Nucleus 8
2. Nucleus 7

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

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 each test session and take-home periods, subjects will return all 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 Performance Evaluations and Procedures

7.3.1 Speech perception in quiet

Speech perception in quiet will be measured using the CNC monosyllabic words (Peterson & Lehiste, 1962) at 50 dB SPL from S0 position. See Figure 3. There will be 2 lists per condition. The goal of speech perception assessment in quiet is to compare % words correct for each of the conditions.

7.3.2 Speech perception in noise

Speech perception in noise will be measured using the Australian Speech Test In Noise (AUSTIN) (Dawson, Hersbach, & Swanson, 2013), which is a test that uses BKB like target sentences presented in adaptive noise. The goal of the speech perception test in noise is to provide the SNR for 50% speech intelligibility. The signal level will be fixed at 65 dB SPL. All sentence in noise tests will be measured using this procedure.

Speech perception performance in noise and quiet will be assessed using a loud-speaker configuration as shown in the diagrams of Figure 3

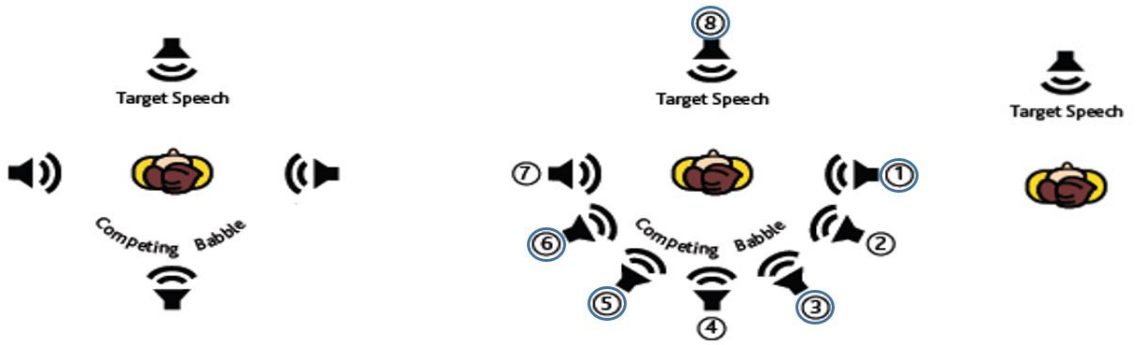

Figure 3. Left – S0N3 with babble noise from 90, 180 and 270 degrees (3 talkers in total). Middle – S0Nrearhalf with roving babble noise presented from 4 speakers in the rear hemisphere (4 talkers in total). The rear hemisphere will consist of 7 speakers and the 4 noise speakers will change for every sentence in the test list. Right – S0 CNC words

7.3.3 Subjective ratings

Baseline Questionnaire – At study entry subjects will be asked a series of questions on their experience with their own sound processor system, including use of and satisfaction with the automatic scene classifier, SCAN, and ForwardFocus.

Nucleus 8 Questionnaire 1 and 2 - After at least 2 weeks of take home use with the Nucleus 8 Sound Processor system, subjects will be asked to return to the study clinic and complete a short list of questions based on the experience with the Nucleus 8 Sound Processor system, including questions on hearing performance, comfort, usability and overall satisfaction. Some questions will be absolute ratings of Nucleus 8 Sound processor, and some will be compared to their experience wearing their own sound processor.

Speech, Spatial and Qualities of Hearing Scale (SSQ12) – The SSQ is designed to measure a range of hearing disabilities across several domains. Subjects are asked to rate their ability to hear speech in a variety of competing contexts, subjects are also asked about their spatial hearing abilities

including the impact of direction, distance and movement associated with spatial hearing. Subjects are also asked about their ease of listening, and the naturalness, clarity and identifiability of different speakers (Gatehouse & Noble, 2004; Noble, Jensen, Naylor, Bhullar, & Akeroyd, 2013). A shortened form of the 49-question SSQ, the SSQ12, will be used in this study.

Study subjects will be asked to complete the SSQ12 at two time points in the study; 1) at study entry, where scores will reflect their experience with their own sound processor, 2) after take home use with the Nucleus 8 Sound Processor.

7.3.4 Usability Assessments

Usability of the Nucleus 8 Sound Processor system may be assessed during study visits and take-home periods. See section 7.3.7 for the procedural provisions relating to usability testing that may be introduced if COVID restrictions are in place during this study period. All subjects will be asked to take part in a usability interview, however participation may be restricted by the video call technology owned by the study subject.

Study subjects may be asked to undertake typical tasks in a simulated use environment and the study investigators will observe the tasks and log any device deficiencies experienced during this time.

7.3.5 Sound Quality

Subjective sound quality assessments with the investigational sound processor may occur during study visits. Handwritten notes will be stored in the subject file and all device deficiencies will be stored in the electronic data base (Medidata Rave). These assessments may be undertaken in real world environments at Cochlear Ltd or on campus at Macquarie University.

7.3.6 Participant Evaluations and Procedures

Visit 0

Included in this period:

- Screening
- Informed consent
- Other standard CRFs including demographics, medical, hearing and device history

Screening and informed consent:

- 20 subjects will be enrolled
- Subjects must be consented to the study and inclusion and exclusion criteria confirmed prior to any study activities starting.

Visit 0 and 1 may be at the same visit.

Visit 1

Included in this period:

- Baseline questionnaire
- SSQ12 – Nucleus 7
- Device fitting
- Sound Quality (optional)
- Usability interview
- Device Deficiencies and Adverse Events

Questionnaires

Based on their experience with their own device, study subjects will be asked to complete the SSQ12 and the baseline questionnaire.

Sound Quality

Depending on the time available and subject willingness, study investigators may ask study subjects to use the investigational medical device in settings at Cochlear Limited, on Campus at Macquarie University or around their home and local areas. Study investigators may ask the study participants questions about the sound quality and general acceptance of the Nucleus 8 (CP1110) Sound Processor system. This informal sound quality assessment may occur before or after the acute speech perception assessment, handwritten notes will be stored in the subject file and all device deficiencies will be stored in the electronic data base (Medidata Rave).

This assessment may occur at any of the study visits.

Take-home use

Recipients will be given 2 programs to use over the next 2 weeks.

P1 = SCANX

P2 = SCAN+FF

Table 3. Take home conditions for SCAN users

	SNR-NR	Directionality	ForwardFocus
P1 Nucleus 8 SCAN X	✓	SCAN	Manual
P2 Nucleus 8 SCAN+FF	✓	SCAN	Automatic

P1 SCANX is similar to the N7 SCAN program where ForwardFocus can be enabled via the Nucleus Smart App. P2 SCAN+FF is the new program where the strength of ForwardFocus and microphone directionality is automatic according to the scene classification. Recipients do not need to manually adjust ForwardFocus when using P2.

Subjects will be encouraged to try both programs in different situations to determine which one they prefer.

For study subjects who do not use, or do not prefer to use, SCAN in their own processor they may be provided with a non-SCAN program in P1.

Non-SCAN users will be provided with:

P1 = Preferred program from N7, either BEAM or Zoom or Standard. Users can select ForwardFocus manually.

P2 SCAN +FF

Table 4. Take home conditions for non-SCAN users

	SNR-NR	Directionality	ForwardFocus
P1 Nucleus 8 Custom	✓	User preference (Standard, Zoom, BEAM)	Manual
P2 Nucleus 8 SCAN+	✓	SCAN	Automatic

At the end of the study visit, the Investigator will set up all devices required for the subject's take-home use. This may include pairing to their own or loaner assistive listening devices, fitting any retention accessories, installing the compatible Nucleus Smart App on subject's own or a loaner smartphone, and pairing the investigational processors to the phone accordingly.

Visit 2

Included in this period:

- Take-home feedback
- Device optimisation including the issuance of new firmware and new features as made available throughout the course of the trial (if required)
- Usability Questionnaire/interview
- Nucleus 8 Questionnaire 1
  SSQ12 – Nucleus 8
- Adverse Events and Device Deficiencies

Take-home feedback

After the take home period, study subjects will be asked about their experience with the Nucleus 8 Sound Processor. The study investigator will optimize the devices if required. Device deficiencies and adverse events experienced during this take home period will be recorded if not already.

Questionnaires

Based on their experience with the Nucleus 8 SP, study subjects will be asked to complete the SSQ12 Questionnaire, usability interview and the Nucleus 8 Questionnaire 1.

Additional usability questions or interviews may be completed during this visit.

Take-home use

At the end of the study visit the Nucleus 8 SP programs will be re-programmed onto the study devices. See instructions under visit 1 ‘Take-home use’ for programs to be used and instructions.

Visit 3

Included in this period:

- Take-home feedback
- Device optimisation including the issuance of new firmware and new features as made available throughout the course of the trial (if required)
- Adverse Events and Device Deficiencies

Take-home feedback

After the take home period, study subjects will be asked about their experience with the Nucleus 8 Sound Processor. The study investigator will optimize the devices if required. Device deficiencies and adverse events experienced during this take home period will be recorded if not already.

Take-home use

At the end of the study visit the Nucleus 8 SP programs will be re-programmed onto the study devices. See instructions under visit 1 ‘Take-home use’ for programs to be used and instructions.

Visit 4

Included in this period:

- Take-home feedback
- Device optimisation including the issuance of new firmware and new features as made available throughout the course of the trial (if required)
- Nucleus 8 Questionnaire 2
- Adverse Events and Device Deficiencies

Take-home feedback

After the take home period, study subjects will be asked about their experience with the Nucleus 8 SP. The study investigator will optimize the devices if required. Device deficiencies and adverse events experienced during this take home period will be recorded if not already.

Questionnaires

Based on their experience with the Nucleus 8 SP, study subjects will be asked to complete the Nucleus 8 Questionnaire 2.

Take-home use

At the end of the study visit the Nucleus 8 SP programs will be re-programmed onto the study devices. See instructions under visit 1 ‘Take-home use’ for programs to be used and instructions.

Additional Visits

During this period of take-home use, between visits 4 and the completion visits. Subjects may come into the clinic or a remote session will be scheduled for device optimisation and troubleshooting, or to receive new features available during development of the product. This visit may include the following:

- Take-home feedback
- Device optimisation including the issuance of new firmware and new features as made available throughout the course of the trial (if required)
- Adverse Events and Device Deficiencies
- Speech Perception Tests (in-clinic only)
    - Sentences in noise
        - S0Nrearhalf
        - S0N3

      Words in quiet (CNC)

Sentence in noise test

See section 7.3.7 for the procedural provisions relating to speech perception testing that will introduced if Covid restrictions are in place during this study period.

Table 5. Speech in Noise test conditions (S0Nrearhalf and S0N3). Whisper, WNR, ADRO and ASC will be activated according to user preference.

	SNR-NR	Directionality	ForwardFocus
Nucleus 8 FF 'Auto'	✓	SCAN	✓
Nucleus 8 SCAN	✓	SCAN	

In booth speech perception testing will be conducted using the signal processing combinations and hardware listed in Table 5. The order of testing will be conducted according to the counterbalancing outlined in Section 7.2.7.

For S0Nrearhalf and S0N3 speech in noise tests, all subjects will be tested in the unilateral condition and each subject will have their contralateral ear (non-test ear) blocked with an ear plug for all test conditions.

The subject will be positioned so that the middle-point of two ears is centred at the reference point of the sound field. The loudspeaker should be positioned at the same height as the middle-point of the two ears.

The AuSTIN software will be used to present the test material. The investigator, or suitably qualified delegate will use the software to select:

- Adaptive test (SRT)

- 65 dB SPL presentation level
- Signal from in front (0 degrees)
- Babble noise from either:
    - S0Nrearhalf: 4 locations in the rear hemisphere
    - S0N3: 90, 180 and 270 (3 speakers in total)

At the beginning of the test session a practice run of 16 sentences with the first signal processing combination to be tested will be undertaken. This practice run is not required to be repeated if all sentence tests are completed on the same day. The starting point for the first test will be set within 5dB SNR of the practice run result. For signal processing parameters that are expected to produce highly variable results or large differences, a practice run may be required for each signal processing combination. The number of sentences will be 20 for all test runs.

The investigator will record the result on the worksheet and in the Electronic Data Capture (EDC) system.

Words in quiet test

In booth speech perception testing will be conducted using the input processing combinations and hardware listed in Table 6. The order of testing will be conducted according to the counterbalancing outlined in Section 7.2.7.

Table 6. Speech in Quiet test conditions. Whisper, WNR, ADRO and ASC will be activated according to user preference.

	SNR-NR	Directionality	ForwardFocus
Nucleus 8	✓	Std	
Nucleus 7	✓	Std	

All subjects will be tested in the unilateral condition and each subject will have their contralateral ear (non-test ear) blocked with an EAR plug for all test conditions. Subjects with bilateral implants that meet the inclusion criteria will be tested using the subject's preferred ear or if the preferred ear is not known then the first implanted ear will be used as the test-ear.

The subject will be positioned so that the middle-point of two ears is centred at the reference point of the sound field. The loudspeaker should be positioned at the same height as the middle-point of the two ears.

The AuSTIN software will be used to present the test material. The investigator, or suitably qualified delegate will use the software to select:

- CNC word test
- 50 dB SPL presentation level
- Signal from in front (0 degrees)
- 2 lists of 50 words each

At the end of each run, the investigator will record the result on the worksheet and in the EDC.

Visit 5 – Completion

- Take-home feedback
- Adverse Events and Device Deficiencies
- Return devices

Take-home feedback

After the take home period, study subjects will be asked about their experience with the Nucleus 8 Sound Processor. The study investigator will optimize the devices if required. Device deficiencies and adverse events experienced during this take home period will be recorded if not already.

Return devices and study completion

At the end of the study, subjects will return to their own device with the commercially available firmware.

Adaptive procedure:

While there are no expected unplanned product changes, early product can be sensitive to the low-risk issues identified in Table 7. During this study these product issues may be identified by study subjects during the in-clinic testing sessions that require optimisation or correction, and an adaptive procedure allows for product feedback to be collected from study subjects, for the product to be updated, and for the updated product to be reissued to study subjects for continued testing. Table 7 identifies how issues will be investigated and retested by the research subjects.

Before initiating speech perception testing, study investigators may ask study subjects to use the investigational medical device in settings at Cochlear Limited or on Campus at Macquarie University.

New Device Iteration:

If a product issue is identified either prior to or during the speech perception evaluation that may have an impact on speech perception outcomes, the formal testing will be paused for subjects while the change is made and a new version of the Sound Processor system will be developed and issued to study participants.

If the product issue was present for all subjects, then all subjects will be asked to repeat any testing that had occurred.

Table 7. Product adaptation categories and product issue examples

Category	Example of a product issue	Action
Sound quality	Study subjects may provide feedback on the general sound quality of the Sound Processor in everyday sound environments like noisy cafes, quiet rooms or windy situations.	If the issue has an impact on performance the product will be updated and speech perception will be re-evaluated by subjects.

	Study subjects may provide feedback that the Sound Processor is unacceptably noisy or has an unacceptably noticeable buzzing.	If the issue has an impact on performance the product will be updated and speech perception will be re-evaluated by subjects.
Intermittency	Study subjects may provide feedback that the Sound Processor is not outputting a consistent signal with gaps in stimulation.	If the issue has an impact on performance the product will be updated and speech perception will be re-evaluated by subjects.
General bugs and product issues:	While all measures have been undertaken to test each of the features with the Nucleus 8 (CP1110) Sound Processor, there may be unforeseen issues that are exposed through usage in the environments used in the study.	General issues will be judged on a case by case basis. If it is judged that the issue has an unacceptable impact on performance, the product will be updated and re-evaluated by subjects.

All product issues will be recorded as device deficiencies. The Sound Processor will be considered mature for speech perception testing when all product optimisations that impact on performance have been made.

Multiplicity and Type I error

This adaptive procedure will only be incorporated when subjective issues are raised by study subjects, and will not be based on the speech perception scores collected during the session.

No repetition of speech perception will occur after the database has been locked. As such, no control of Type I error is necessary when sound quality or intermittencies are identified during data collection.

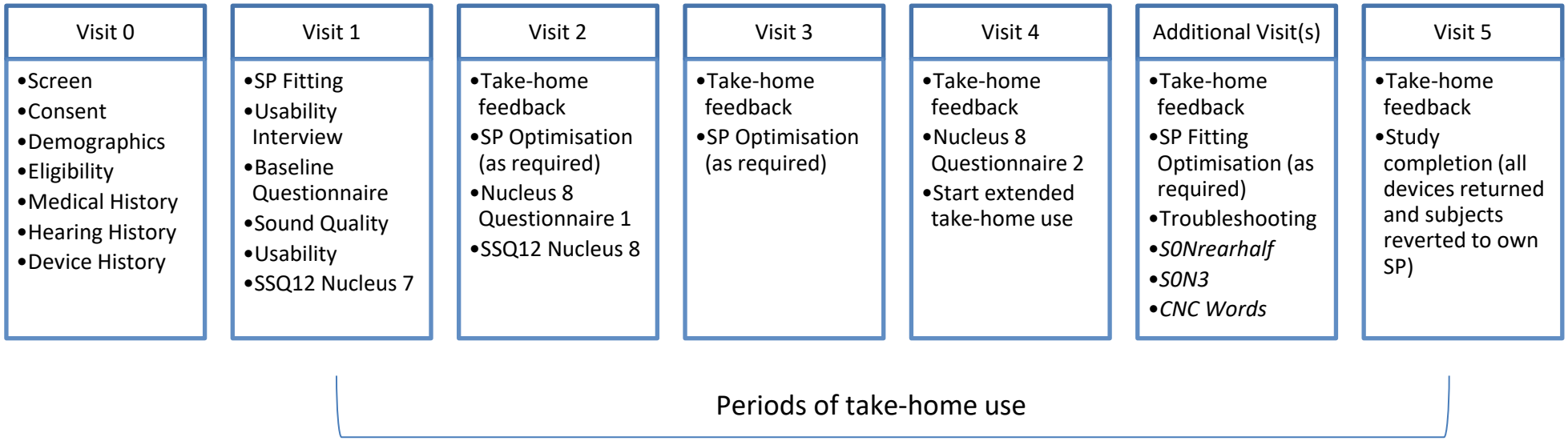

Figure 4. Overview of planned visits

7.3.7 Procedural mitigation relating to COVID-19

Due to the physical distancing restrictions in place during the COVID-19 pandemic, optional device programming and procedural provisions may be introduced. These measures are to support the continuation of this project, while ensuring the safety of subjects and study staff.

- Screening and consent: See section 10 for the consent process. If COVID-19 restrictions also restrict research candidates from attending the study site, screening and consent may be performed via phone call or video conference. Paper copies of the consent form will be provided via mail/courier and subjects will be asked to use a prepaid envelope to return one original signed copy to the site.
- Device programming: Subjects may be asked to commence take-home testing through remote management. Devices, accessories, questionnaires, and instructions may be sent to subjects via courier, so that they do not need to attend the clinic. Prior to shipping, each subject's Nucleus 8 study sound processor(s) will be connected to the fitting software, Custom Sound Pro. The subject's MAP(s) from their own processor(s) are saved in their individual Custom Sound Pro file. This will be converted to their Nucleus 8 sound processor MAP(s), and their preferred programs written to the study processor. If a subject's most recent MAP(s) are not retrievable either from the site's database or the subject's clinical audiologist, remote management will not be possible until they are able to attend the site to have their own processor(s) connected to the software. For subjects who do not wish to participate in remote study and device management, the device programming and fitting will be performed in clinic once restrictions in New South Wales are eased.
- Usability interviews: Usability assessments may be conducted remotely to accommodate situations where test participants are unable to, or would prefer not to, travel to a site in order to perform testing. In the remote scenario, the usability interview will be conducted via video conferencing software. Subjects will be provided with all devices, accessories and user manuals required for the testing.
- Speech perception**:** Speech perception testing can only be conducted at the study sites. If restrictions are ongoing at the planned time of these study visits, these tests may be moved to later in the study. As such, speech perception tests have been decoupled from specific visits. If time permits, and study subjects are willing, all speech perception tests may be conducted on the same day. All comparisons for a specific endpoint test will be completed on the same day.

7.4 Safety Evaluations and Procedures

The risks and anticipated ADEs for the Nucleus 8 SP, 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 may be conducted by the Sponsor's Medical Officer in accordance with the Sponsor's standard operating procedures.

7.4.1 Concomitant Medication and Therapies

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

7.5 Equipment Used for Evaluation of Performance and Safety

7.5.1 Software

Speech testing in quiet and noise will be performed via the adaptive Australian Sentence Test in Noise (AuSTIN) test software (Dawson et al., 2013)

Devices and signal processing configurations will be programmed using Custom Sound 7.0.

7.5.2 Speech Perception

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

Speech perception performance in noise will be assessed using a loudspeaker configuration with the speech from the front and noise from four roving locations in the rear hemisphere (S0Nrearhalf) and with speech from in front and noise from 90, 180 and 270 degrees azimuth (S0N3).

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

7.5.3 Questionnaires

Subjective ratings of the test sound processors will be evaluated via paper-based questionnaires.

7.6 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. Investigators are qualified audiologists familiar with cochlear implant development, surgery and programming. Investigators' trial materials, programming and testing rooms (sound booths) are securely separated from Sponsor facilities. The trial investigators, or delegates within the study site, will enter the data into the eCRF.

The study is planned, designed and developed by a separate group within Cochlear, known as Clinical Affairs (the Sponsor). Cochlear has SOPs to manage the separation of Investigator and Sponsor activities as well as ensure they align with all applicable regulations.

Activities to be performed by sponsor representative excluding monitoring include:

1. Application of clinical quality assurance and quality control principles to the processes of the clinical investigation
    a. Implement and maintain written clinical quality procedures to ensure the clinical investigation is designed, conducted and that data generated is compliant with the ISO 14155:2011 Standard (ISO, 2011).
    b. Clinical quality assurance and quality control will be implemented according to sponsors quality system (Cochlear Quality Manual reference [7])
2. Clinical investigation planning and conduct

a. Selection of clinical personnel for project management of the clinical investigation
b. Preparation of documents and materials for the clinical investigation
c. Project management for the clinical investigation. i.e. accountability of investigational devices, clinical trial insurance coverage, submission of application(s) and investigation updates to the appropriate regulatory authority(ies).

3. Safety evaluation and reporting of adverse events (AE) to the TGA and ethics committee
4. Clinical investigation close-out, statistical analyses and final report

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

8.1 Anticipated Clinical Benefits

This study provides subjects with the opportunity to trial a new cochlear implant sound processor and related components (Nucleus 8) prior to the commercial release date. Subjects may benefit from improved usability and performance of the different components of the Nucleus 8 system. For subjects who have not previously experienced using the ForwardFocus feature, they may experience benefit of improved communication through reduction of distracting background noise.

Due to the limited use of the IMD (minimum of 4 test blocks over a period of up to 12 months), there are no long-term clinical benefits anticipated for the subjects.

8.2 Anticipated Adverse Device Effects

Cochlear's internal hazards analysis considers probable hazardous situations relating to the Nucleus 7 and Nucleus 8 SPs.

The risks associated with the Nucleus 7 and Nucleus 8 SPs and Accessories have been identified, analysed and evaluated. The residual risk level has been determined to be as low as possible in accordance with Cochlear's Product Risk Management Procedure and are acceptable.

Subjects may be exposed to the anticipated adverse device related effects associated with use of the Nucleus 7 and Nucleus 8 SPs such as pain or discomfort when wearing the processor and a risk that some sounds could be uncomfortable. Product specific warnings can be found in the respective User Guide and relevant instructions for use.

8.3 Risks Associated with Participation in the Clinical Investigation

There is a small risk that the programs on the Nucleus 7 SP and Nucleus 8 SP may sound different to subjects own SP. If subjects experience sound that is uncomfortable they are counselled to remove the sound processor off their head or ask the research audiologist to immediately cease stimulation. Other risks may include exacerbation of existing tinnitus and a reduction in the sound quality or intelligibility of the research programs. Subjects are advised to return to their own processor and promptly inform the investigators if these events occur. Possible interactions with concomitant medications and residual risks for the device are not anticipated in this clinical investigation.

See the Nucleus 7 SP User Guide for all Warnings and Contraindications. (user guides can be found within the 'Support' section of the country specific Cochlear website; [redacted]). At this preliminary stage in development, the Nucleus 7 SP User Guide will be relevant for Nucleus 8 SP.

As the study procedures involve planned visits to the Cochlear headquarters research site, there may be an increased risk of contracting infectious diseases such as COVID-19 whether in transit to the site or moving throughout the building.

8.4 Risk Mitigation

The study investigational devices have been tested for safety, and the performance and use of the device is expected to be similar to the approved Nucleus 7 SP. Risks have been individually reviewed and found to be clinically acceptable based on implemented controls, verification activities, and the relatively low probability of harm. One or more of the following risk control options are applied to each identified risk: inherent safety by design; protective measures in the device itself or in the manufacturing process; Information for safe usage.

The fitting and use of the CP1110 SP will be managed by the investigator. In cases where the sound becomes at all uncomfortable or uncomfortably loud during fitting, subjects are encouraged to remove the SP from their head or inform the investigator so that stimulation is immediately ceased. Should any such discomfort occur during take-home use, subjects will be advised to remove the CP1110 SP and revert to using their own SP until the cause of the discomfort is understood and resolved.

If subjects experience any physical discomfort from the device or if the device produces sounds that are uncomfortable, subjects are encouraged to inform the Investigator and return to using their own sound processor.

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.

Risk mitigation relating to COVID-19

It is expected that study participants will be taking steps to limit exposure to infectious diseases, for example, COVID-19. The site will actively follow the advice of official health authorities and governments to ensure the health and wellbeing of site employees and research subjects. These include but are not limited to:

- Operational changes to ensure attendance at the site is limited to only those who are required to be there. Cochlear headquarters has implemented procedures to enable contact tracing for all employees and visitors, as well as processes to scale up, scale down and/or deep clean should there be a confirmed positive case of the virus on the premises.
- The research site is separated physically, enabling separation of study participants from other employees working in the building.
- Increased hygiene etiquette including cleaning of high-touch surfaces before and after each study visit, disinfection of any shared study devices or equipment and investigators are equipped to use gloves or wear a face masks as required. Hygiene

resources such as handwashing/rubbing stations are readily available throughout the building and research site.

- Where possible, study participants will be encouraged to drive to Cochlear and utilise free on-site parking instead of travelling via public transport.
- Subjects will be provided with any necessary resources required to return study devices to the site, should they be unable to attend any of the planned visits. For example, couriers or postage may be arranged as necessary.

8.5 Risk-to-Benefit Rationale

Residual risk levels associated with the CP1110 SP and accessories have been determined to be as low as possible when the sound processor is used with a compatible cochlear implant. The probability of occurrence of harm for all hazards was found to be “remote” or “improbable”. Based on pre-clinical testing of the CP1110 SP along with a review of clinical investigations and published data on the Nucleus 7 SP, the anticipated clinical benefits have been found to outweigh the potential risks to the subject through participation in this clinical investigation.

9 STATISTICAL CONSIDERATIONS

9.1 General Considerations

See sections 9.2 to 9.10 for statistical considerations.

9.2 Endpoints

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.

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 SSQ12 endpoint, one 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 Questionnaires, Nucleus 8 Questionnaires 1 and 2 and the Baseline Questionnaire, the endpoint is the completion of the questionnaire.

9.2.1 Primary Endpoint

The primary efficacy measure for the Nucleus 8 Sound Processor will be Speech Reception Thresholds (SRT) assessed via AuSTIN Sentence scores in spatially separated adaptive noise.

The primary efficacy outcome for the study will be determined by the following primary efficacy endpoint:

- Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus ON (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0Nrearhalf 4TB).

9.2.2 Secondary Endpoints

- Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus On (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0N3 Babble).
- Paired difference in percentage CNC Words correct in quiet (50 dB) with the CP1110 Sound Processor and Nucleus 7 Sound Processor
- Paired difference in Global SSQ12 scores after experience with the CP1110 Sound Processor and Nucleus 7 Sound Processor
- Ratings on the 'CP1110 Questionnaire 1' and 'CP1110 Questionnaire 2' after at least 2 weeks of experience with the CP1110 Sound Processor
- Take home use with the CP1110 Sound Processor System

9.2.3 Exploratory Endpoints

Feedback from take home use with the CP1110 Sound Processor System.

9.3 Hypotheses

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.

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 SSQ12 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 -1, the treatment condition is regarded as non-inferior to the control on that measure.

9.3.1 Primary Hypothesis

Endpoint: Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus ON (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0Nrearhalf 4TB).

H0: Sentence in noise (S0Nrearhalf 4TB) scores (dB SRT) with the CP1110 Sound Processor with FF On (treatment) are inferior to those with the CP1110 Sound Processor with FF Off (control)

CP1110 *FF ON* – CP1110 *FF OFF* ≥ *1 dB (NB: higher SRT scores represent poorer performance)*

H1: Sentence in noise (S0Nrearhalf 4TB) scores (dB SRT) with the CP1110 Sound Processor with FF On (treatment) are non-inferior to those with the CP1110 Sound Processor with FF Off (control)

CP1110 *FF ON* – CP1110 *FF OFF* < 1 dB

9.3.2 Secondary Hypotheses

Secondary endpoint 1

Endpoint: Paired difference in dB SRT (AuSTIN) between the CP1110 Sound Processor with ForwardFocus On (SCAN) and ForwardFocus OFF (SCAN) (65 dB SPL S0N3 Babble).

H0: Sentence in noise (S0N3 Babble) scores (dB SRT) with the CP1110 Sound Processor with FF On (treatment) are inferior to those with the CP1110 Sound Processor with FF Off (control)

CP1110 *FF ON* – CP1110 *FF OFF* ≥ *1 dB*

H1: Sentence in noise (S0N3 Babble) scores (dB SRT) with the CP1110 Sound Processor with FF On (treatment) are non-inferior to those with the CP1110 Sound Processor with FF Off (control)

CP1110 *FF ON* – CP1110 *FF OFF* < 1 dB

Secondary endpoint 2

Endpoint: Paired difference in percentage CNC Words correct in quiet (50 dB) with the CP1110 Sound Processor and Nucleus 7 Sound Processor

H0: Words in quiet (50 dB CNC words) scores (% words correct) with the CP1110 Sound Processor (treatment) are inferior to those with the Nucleus 7 Sound Processor

CP1110 – Nucleus 7 ≤ -10%

H1: Words in quiet (50 dB CNC words) scores (% words correct) with the CP1110 Sound Processor are non-inferior to those with the Nucleus 7 Sound Processor

CP1110 – Nucleus 7 > -10%

Secondary endpoint 3

Endpoint: Paired difference in Global SSQ12 scores after experience with the CP1110 Sound Processor and Nucleus 7 Sound Processor

H0: Hearing performance ratings (SSQ12) with the CP1110 Sound Processor (treatment) are inferior to those with subject's own processor (control)

CP1110 – Nucleus 7 ≤ -1

H1: Hearing performance ratings (SSQ12) with the CP1110 Sound Processor (treatment) are non-inferior to those with subject's own processor (control)

CP1110 – Nucleus 7 > -1

There are not hypotheses for the following endpoints;

- Ratings on the 'CP1110 Questionnaire 1' and 'CP1110 Questionnaire 2' after at least 2 weeks of experience with the Nucleus 8 Sound Processor
- Take home use with the CP1110 Sound Processor System

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 SRT (Speech Recognition Threshold) scores and CNC word scores. The sample size using a confidence interval method (one-tailed 97.5% confidence interval) was estimated to have a reasonable power to detect non-inferiority of sentence and word scores for the above-mentioned hypotheses.

To reject the null hypothesis of inferior sentence in noise scores (SRT scores), the following parameters for sample size calculation were chosen:

- A clinical important difference value of 1 dB SRT. This margin is based on clinical consensus. NB: *higher SRT scores represent poorer performance*.
- A standard deviation (SD) of change or difference scores of 1.36 dB. This SD is calculated from 256 paired differences and is an indicative test re-test SD for both S0N3 and S0N0.
- A significance level $\alpha = 0.025$ (one-tailed).
- A desired power of 0.8

Based on these assumptions, a sample size of 17 are required to reject the null hypotheses. Twenty subjects will be enrolled to allow for any unforeseen subject withdrawal.

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 treatment 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 treatments and have at least one set of paired treatment and control 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 treatments and have at least one paired measurements from treatment and control, without major protocol deviations. Major deviations will be defined at the clean file meeting before data base lock.

It is possible that a treatment 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 treated subjects. The Safety Population will be used for the safety data analysis.

9.6 Primary Endpoint Analyses

Primary and Secondary Speech Perception Endpoints:

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 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.

The same analysis method will be applied to the non-inferiority test for words in quiet scores (monosyllables). 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.

Only when the non-inferiority test for the above specified endpoint is successful, then a superiority test for the endpoint will be further conducted to assess the treatment effect.

9.7 Secondary Endpoint Analyses

SSQ12 and other questionnaire 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.

For the non-inferiority test of Global SSQ12 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 -1, the treatment condition is regarded as non-inferior to the control.

Data from the other questionnaires including the results for individual questions on the SSQ 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.

9.8 Exploratory Endpoint Analyses

Not applicable

9.9 Safety Analyses

For AE/ADEs and DDs, the percentage of subjects who experienced at least one occurrence of each, will be summarised by intervention group. Any 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.

9.10 Interim Analyses

After the first take home period with the Nucleus 8 SP system, an analysis is planned on the following tests and comparisons:

- Speech perception in noise (S0Nrearhalf, S0N3)
- Baseline Questionnaire and Demographics
- Nucleus 8 Questionnaire 1
- Usability Assessment
- Adverse Events and Device Deficiencies at the point of interim database lock

This analysis will include the complete data set for the primary endpoint, as such no multiplicity adjustment will be made for this analysis as all data for the outcome measures outlined above will be analysed together. It is not anticipated that these results will have an unacceptable influence on the remainder of the trial.

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 risks and benefits, what participation will involve, and alternatives to participation will be explained 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.

Each subject (or their legally authorised representative) and the person who conducted the informed consent discussion, shall sign and date the Informed Consent Form (ICF). Where required, a 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.

The subject, or the subject's legally authorised 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.

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 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.

11.1.3 Serious Adverse Event

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

1) led to a death,

2) led to a serious deterioration in the health of the subject that either resulted in:

- a life-threatening illness or injury, or
- a permanent impairment of, or damage to, a body structure or a body function, 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, or
- Chronic disease.

3) led to foetal distress, foetal death or a congenital physical or mental abnormality, or birth defect

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 Investigator's Brochure.

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

11.1.6 Device Deficiency

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

NOTE: Device Deficiencies include malfunctions, use errors, and inadequate labelling or information supplied by the manufacturer.

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, and/or SADEs 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 risk analysis report, 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 and/or the Investigator's Brochure 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) a) suitable action had not been taken,
2) b) intervention had not been made, or,
3) c) 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, must be reported to the Sponsor within 5 working days.

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.

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, and shall conduct an expedited assessment of all SAEs, unanticipated ADEs, DDs that could have led to an SADE.

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

Name of Sponsor Safety Monitor	Clinical Review Board
Country and time zone:	Australia, Australian Eastern Standard Time
Phone number:	NA
Email:	[redacted]

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 10 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 sound processors. As this study is an open label study, no Independent Data Monitoring Committee (IDMC) has been established for this clinical investigation.

12 Device Accountability

Supply of investigational medical devices will be recorded using the Sponsor Device Tracking Form and Software Tracking Form by the sponsor representative. Investigational medical device(s) 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 Sponsor's Individual Subject Accountability Log Form by the principal investigator.

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 unused medical devices shall be returned to the Sponsor.

Contact information regarding the IMD and/or comparator is provided below.

Name of contact person of the Sponsor:	[redacted]
Country and time zone:	Australia, Australian Eastern Standard Time
Phone number:	[redacted]
Email:	[redacted]

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.

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.

Data collection will be performed using [redacted] for electronic data capture (EDC) 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.

[redacted] uses 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.

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

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 10 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 at a public clinical trial registry ClinicalTrials.gov.

Investigators will be able to publish and/or present the data generated from the clinical investigation after mutual agreement between the Coordinating Investigator, the Principal Investigators, and the Sponsor prior to investigation start. Manuscript authorship and responsibilities will be in accordance with guidelines and recommendations provided by the International Committee of Medical Journal Editors (ICMJE) to enable communication in a timely manner. 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, International Standard ISO 14155 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 describing all the activities performed during monitoring, and close out.

Monitoring activities may be performed by Avania CRO according to a pre-approved Statement of Work

22.2 Audits

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.

23 TRADEMARKS AND COPYRIGHT

24 REFERENCES

Dawson, P. W., Hersbach, A. A., & Swanson, B. A. (2013). An adaptive Australian Sentence Test in Noise (AuSTIN). *Ear and Hearing*, *34*(5), 592–600. https://doi.org/10.1097/AUD.0b013e31828576fb

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International Organization for Standardization. ISO 14155:2011 Standard: Clinical investigation of medical devices for human subjects – Good clinical practice. 2011. Available at: https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-2:v1:en

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Peterson, G. E., & Lehiste, I. (1962). Revised CNC lists for auditory tests. *The Journal of Speech and Hearing Disorders*, *27*(February), 62–70. https://doi.org/10.1044/jshd.2701.62

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World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 2013. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.

25 CHANGE HISTORY

Version	Change	Rationale
1.0	1) Introduction of the document 2) Boiler plate wording for exclusion criteria has been changed to "Currently participating or participated in another interventional clinical study/trial in the past 30 days, or if less than 30 days, the prior investigation was Cochlear sponsored and determined by the investigator to not impact clinical findings of this investigation". 3) Section 7.2.6 regarding criteria for withdrawal has been changed to "Subjects…are not obliged to provide any justification for their decision:.	1) N/a 2) Since the study will run at an internal site, the investigators would be able to determine if this is suitable as they have access to knowledge about that prior investigation. 3) Bellberry HREC requires clarification that subjects can withdraw from the study without providing any reason or justification to the Investigator.
2.0	1) Addition details on the covid-related provisions as a result of the ongoing restrictions in place in NSW, including the procedures for remote consent, remote issuance of questionnaires, and remote usability testing. Further clarity also provided around the flexibility for in-booth speech perception to occur at a later study visit. 2) Exploratory endpoint changed from "confirm" to "evaluate". 3) Section 19: retention period updated to *minimum 10 years* to match PICF.	1) Restrictions on travel and gatherings of persons are in place due to the COVID-19 global pandemic and procedural provisions and mitigations have been introduced to allow for the study to proceed. 2) Requested by Bellberry HREC. 3) Cochlear Quality Records Register requires 15 years as the minimum for implants, 10 years for externals. Wording updated to match the PICF, which was previously approved by Legal.

APPENDIX 1: STATEMENT/DECLARATION OF DEVICE CONFORMITY

Cochlear®

QMS Document

STATEMENT OF CONFORMITY FOR UNAPPROVED DEVICE

Clinical Investigation Details:

Clinical Investigation ID:	CLTD5810
Sponsor of Investigation:	Cochlear Limited, 1 University Avenue, Macquarie University, NSW 2109, Australia

Device and Manufacturer Details:

Device Manufacturer:	Cochlear Limited, 1 University Avenue, Macquarie University, NSW 2109, Australia
Investigational Device:	Nucleus 8 System

We, Cochlear Limited, declare that where appropriate technical and biological and pre-clinical evaluations have been conducted, and as a result the investigational device(s) conforms to the applicable general safety and performance requirements (as specified in Annex I of Regulation (EU) 2017/745), apart from the aspects covered by the clinical investigation and that, with regard to those aspects, every precaution has been taken to protect the health and safety of the subjects, the users and third persons.

The Device incorporates no materials of animal or human origin.

All supporting documentation is retained under the premises of the manufacturer.

Name:	[redacted]
Position:	Director of Regulatory Affairs
Signature:	[redacted]
Date:	14th July, 2021

Template 1419103 Version 1.0 1 of 1

Signature Page for VV-TMF-06258 v2.0

Reason for signing: Approved	Name: [redacted] Role: A Date of signature: 31-Aug-2021 00:31:18 GMT+0000

Signature Page for VV-TMF-06258 v2.0