Clinical Investigation Plan

Investigation Title: A Pre-Marketing, Prospective, Single-Site, Open-Label, Within-Subject, Pilot, Interventional Study of Adult Cochlear Implant Speech Perception with the Kanso 2 (CP1150) Sound Processor Compared with the Next Generation of Signal Processing Technology

Short Title: **OPTIMUM**

CIP Number: **CLTD5818**

Sponsor **Cochlear Limited**
1 University Avenue
Macquarie University, NSW 2109
Australia
[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: NCT05286385

Manufacturer	Cochlear Limited 1 University Avenue Macquarie University, NSW 2109 Australia
Sponsor Organisations	Cochlear Limited 1 University Avenue Macquarie University, NSW 2109 Australia
Principal Investigator	[redacted] Principal Research Audiologist Cochlear Limited 1 University Avenue, Macquarie University, NSW 2190
Clinical Research Organisation	[redacted]
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**

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1 DEFINITIONS AND ABBREVIATIONS

Term	Description
ADE	Adverse Device Effect
ADRO	Adaptive Dynamic Range Optimisation
AE	Adverse Event
AMDT	Approved Medical Device on Test
AuSTIN	Australian Speech Test In Noise
BEAM	Adaptive Beamformer
BTE	Behind The Ear
BLE	Bluetooth Low Energy
CER	Clinical Evaluation Report
CI	Cochlear Implant
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CNC	Consonant Nucleus Consonant
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
EDC	Electronic Data Capture
FF	Forward Focus
GCP	Good Clinical Practices
IB	Investigator's Brochure
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
IMD	Investigational Medical Device
ITT	Intent-To-Treat (ITT) and
NCA	National Competent Authority
NFS	Nucleus Fitting Software
NF	Notch Filter

Term	Description
OTE	Off-the-Ear
PI	Principal Investigator
PIL	Principal Investigator List
PMS	Post-Market Surveillance
PP	Per Protocol
RF	Radio Frequency
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SNR-NR	Signal to Noise Ratio- Noise Reduction
SOP	Standard Operating Procedure
SRT	Speech Reception Threshold
SSQ	Speech, Spatial and Qualities
std	Standard directionality
SWN	Speech Weighted Noise
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A Pre-Marketing, Prospective, Single-Site, Open-Label, Within-Subject, Pilot, Interventional Study of Adult Cochlear Implant Speech Perception with the Kanso 2 (CP1150) Sound Processor Compared with the Next Generation of Signal Processing Technology
Short title	OPTIMUM Study
Investigation number	CLTD5818
Name of investigational medical device(s)	• Kanso 2 Notch Filter (NF) Sound Processor • Kanso 2 Sound Processor with Forward Focus (FF) • CDI Tool Version 7.3.1(used in conjunction with Kanso 2 Sound Processors for programming NF and FF to device) • Nucleus 8 (CP1110) Sound Processor (Unapproved device)
Intended use of investigational medical device(s)	The intended use and indications for use for the Kanso 2 NF Sound Processor is the same as the Kanso 2 (CP1150) Sound Processor. **Intended Use**: The Kanso 2 NF Sound Processor is intended to restore a level of meaningful hearing by capturing environmental acoustic sounds and/or sound from auxiliary wireless devices; processing the audio and communicating the processed audio to a compatible implant to provide electrical stimulation to the cochlea, or electrical stimulation of the auditory brainstem. While the Kanso 2 NF Sound Processor is intended to be compatible and can be used with Hybrid implants it is not intended to provide acoustic stimulation. **Medical Indications for Use**: The Kanso 2 NF Sound Processor requires a compatible Cochlear implant, see listed below: • Freedom Hybrid: CI24RE (H), CI24RE (S) • Freedom Series Implants: CI24RE (ST), CI24RE (CA), CI24RE (CS), CI422 • CI600 Series Implants : CI612, CI613, CI622, CI624 • CI500 Series Implants : CI512, CI513, CI522, CI532, CI551 Double Array and ABI541 • N24 Series Implants: CI24R (CS), CI24R (CA), CI24R (ST), CI24M, CI11+11+2M, CI24MH (also known as CI6+16+2M) and ABI24M
Name and description of comparator device/product(s)	• Kanso 2 (CP1150) Sound Processor • Custom Sound Pro 6.3 The Nucleus 8 and Kanso 2 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.

Estimated recruitment period	4 weeks
Expected duration per subject	1 visit, no visit window
Number of subjects planned	9-12
Number of investigational sites planned	1 – Cochlear Limited, Sydney
Inclusion criteria	1) Aged 18 years or older 2) Post lingually deafened 3) Implanted with the CI600 Series, CI500 Series or Freedom Series 4) At least 6 months experience with a cochlear implant. 5) At least 3 months experience with a Nucleus 6 (CP910/920), Kanso (CP950), Kanso 2 (CP1150), or Nucleus 7 (CP1000) Sound Processor 6) MAP Total Stimulation Rate of 7.2kHz or greater 7) Able to score 30% or more with CI alone on a monosyllabic words in quiet test 8) Willingness to participate in and to comply with all requirements of the protocol 9) Fluent speaker in English as determined by the investigator 10) Willing and able to provide written informed consent
Exclusion criteria	1) Additional disabilities that would prevent participation in evaluations. 2) Implant location that would result in undesirable hearing performance or discomfort with an off-the-ear sound processor, as determined by the investigator. 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 unless (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) Implanted with other active implantable medical devices (e.g. pacemaker, defibrillator).

Objectives and Endpoints	
Primary Objective	**Primary Endpoints**
To evaluate the impact of NF on adult cochlear implant recipient's speech perception in quiet using an off-the-ear (OTE) Sound Processor	Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 (CP1150) Sound Processor and Kanso 2 NF Sound Processor
Secondary Objectives	**Secondary Endpoints**
To evaluate the performance of Forward Focus (FF) combined with standard microphone directionality on adult cochlear implant recipient's speech perception in quiet using an OTE Sound Processor	Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 (CP1150) Sound Processor and Kanso 2 Sound Processor with FF
To compare adult cochlear implant recipient's speech perception in quiet with Kanso 2 and Nucleus 8 Sound Processors	Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 (CP1150) Sound Processor and Nucleus 8 Sound Processor
Exploratory Objective	**Exploratory Endpoint**
To characterise the impact of NF on adult cochlear implant recipient's phoneme perception in quiet using an OTE Sound Processor	Paired difference in percentage phonemes correct in quiet (50 dB) with the Kanso 2 (CP1150) Sound Processor and Kanso 2 NF Sound Processor

3 SCHEDULE OF EVENTS

All visits can take place on the same day.

Visit Type	Screening	Visit 1	EOS
Procedures			
Written informed consent	X		
Eligibility	X		
Sentence in babble test (+15 SNR)	X*		
Demographics	X		
Hearing history	X		
Device history	X		
Medical history	X		
Device fitting		X	
Speech perception testing – Words in Quiet 50 dB		X	
Concomitant medications/therapies		X	X
Adverse events		X	X
Device deficiencies		X	X
Device exposure		X	X

*If required

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

This clinical study aims to investigate speech performance in quiet with a Kanso 2 NF Sound Processor that has modified firmware incorporating notch filters at 978Hz, 1956Hz, 2934Hz, 3912Hz compared with the commercially available Kanso 2 (CP1150). The study also investigates Nucleus 8 and and Kanso 2 with FF.

This study will build on the evidence collected in previous Nucleus 7, Nucleus 8 and Kanso 2 clinical studies (see section 4.2.2), and will inform design decisions for future Sound Processors, including decisions relating to future implant compatibility and signal processing automation.

4.2 Findings of Previous Nonclinical and Clinical Studies

4.2.1 Nonclinical Data

[redacted]

[redacted]

4.2.2 Clinical Data

Clinical data relevant for the current investigation fall under two main categories 1) Evidence on the development and approval of FF and 2) Evidence on previous OTE SP generation. These clinical data are summarized below:

FF 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 Signal to Noise Ratio – Noise Reduction (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, FF 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 FF. The two noise reduction algorithms complement each other due to their different principles of operation. Hersbach et al. (2013) found that FF provided a significant improvement in group mean speech reception threshold compared with BEAM.

A clinical evaluation of FF performance (CRC5513), using the Nucleus 6 Sound Processor (Model CP910), revealed higher group mean speech perception scores with FF (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 FF 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 FF than with Standard, Zoom or Beam(Z). There was no significant group difference in Speech, Spatial and Qualities (SSQ) rating between FF and the comparator programs (Standard, Zoom or Beam(Z)). There was an overall preference for SCAN with FF over SCAN alone. The investigators concluded that FF 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 FF 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 FF programs than N6 SCAN. Word recognition scores in quiet and questionnaire ratings for all FF 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 FF only. A decrement compared with FF Strong was found. Sentence in noise scores with speech presented to the cochlear implant side or from behind the listener with mild FF were inferior to the baseline. Based on these findings the investigators recommended that FF be introduced as a custom programme that could be selected for specific listening conditions.

Study CLTD5606 was designed to assess the effectiveness of FF 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 FF (strong, medium and mild) were found to be superior to the Nucleus 6 SCAN. For SWN presented behind the listener FF Strong was demonstrated to be superior to the Nucleus 6 SCAN. When speech and either SWN or four-taker babble were co-located in front of the listener, sentence recognition with FF strong was similar to the Nucleus 6 SCAN. For CNC words in quiet FF Strong was inferior to the Nucleus 6 SCAN. The investigators concluded that acceptable performance and safety of the FF program can be anticipated for Nucleus 7 SP users in noisy environments, and the risk versus benefit profile is acceptable when FF be used in quiet environments.

The in-house study CLTD5709 investigated the effect of FF 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 FF On was superior to FF 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 FF On and FF Off, and therefore no difference in listening effort.

Questions from the Speech domain of the 'SSQ of Hearing Scale' and 3 questions from the Qualities of Hearing domain were completed by subjects at baseline and after at least 4 weeks of use with FF. 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 FF. The majority of respondents found the FF controls within the Nucleus Smart App as very easy to use and half of the respondents wanted FF on their own processor.

Clinical Data for OTE Sound Processors

The main relevant study with an OTE Sound Processor is the CLTD5754 study, the primary objective of this study was to determine the feasibility of FF in an OTE configuration and the secondary objective was to collect formative usability information with prototype and early design versions of the Kanso 2 (CP1150) Sound Processor.

Twenty-two adult subjects underwent speech perception testing using Australian Speech Test In Noise (AuSTIN) adaptive sentences presented from the front with 4 talker babble noise from 90,180 & 270 degrees to the subject (S0N3). AuSTIN Speech Reception Threshold (SRT) data comparing FF ON and FF OFF demonstrated superiority with FF ON (P=0.002, paired t-test).

The implementation of FF in the CLTD5754 included the fixed microphone directionality Zoom and no automation. This evidence supported the approval of FF with the Kanso 2 Sound Processor.

4.3 Study Rationale

This investigation is planned to evaluate the performance of signal processing additions and features that may be new to a future version of the OTE Sound Processor. This study will build on the evidence previously collected on OTE and behind-the-ear (BTE) Sound Processors and will support the design goals for access to the same sound processing algorithms across future OTE and BTE variants, including evidence required on the automation of FF and future implant compatibility. This

study is intended to assess the clinical impact of the design choices made to achieve these future design goals, including:

- **Future implant compatibility:** As a result of the proximity of the split link RF coil to the acoustic electronics, noise has been measured on the bench with an OTE coupled to a future implant design. This study will investigate whether the proposed notch filters have an impact on performance in quiet compared to a current commercially available OTE (Kanso 2).
- **Automation of ForwardFocus on an OTE Sound Processor:** Previous BTE studies have shown a small decrement in speech perception in quiet with ForwardFocus compared to no ForwardFocus (D1376556), however parameter changes and automation have been implemented to resolve this issue, including the reduction in strength of FF and the inclusion of the standard directionality (std) in the 'Quiet' class. This study will assess whether FF (moderate)+standard directionality provides acceptable performance in quiet compared to the current commercially available Kanso 2 with FF.
- **Kanso 3 vs Nucleus 8 Claim –** The study also aims to provide confirmatory evidence on the comparability of OTE and BTE Sound Processors in quiet.

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)

5.1.1 Kanso 2 and Kanso 2 NF Sound Processor

The Kanso 2 (CP1150) Sound Processor is the latest commercially available OTE Sound Processor from Cochlear Limited and provides an alternative form factor with similar functionality to current BTE Sound Processors. Functionality of the is enabled by the NEO-XS processing chip, which is also used in the current, approved (Nucleus 7) BTE processor.

The Kanso 2 NF Sound Processor is identical to the Kanso 2 Sound Processor with the addition of notch filters at 978Hz, 1956Hz, 2934Hz, 3912Hz. The principal architectural difference between OTE processors such as the CP1150 and BTE Sound Processors from Cochlear is that the RF coil that supplies power and data to the internal implant is housed within the processor, rather than in a separate unit connected by a cable to a BTE processing unit. The CP1150 is smaller than the existing CP950 (Kanso) OTE Sound Processor and delivers additional functionality. The external appearance and internal layout of the CP1150 are shown in Figure 4 and Figure 5.

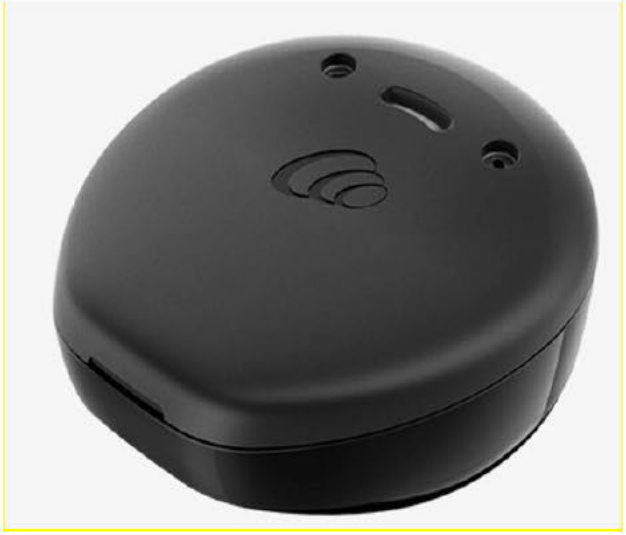

Figure 4: External view of the Kanso 2 (CP1150) Sound Processor

Sound is detected by two microphones placed symmetrically on the outer surface of the processor and protected from dirt and debris by a replaceable microphone cover. [redacted] The external processor is aligned with the internal implant receiver coil by a magnet, which is available in different strengths to accommodate varying user hair types and skin thicknesses. Standard axial magnets are available in seven strengths and imaging (I) diametric magnets, used with CI600-series

implants, are available in six strengths to prevent magnets becoming a choking hazard for small children, the magnets are designed to be tamper resistant and can only be removed from the Sound Processors using a specialised tool.

Unlike the CP950 (Kanso) and CP1000 (Nucleus 7) devices, the CP1150 has no control button. The processor is turned on by double-tapping the Cochlear logo on the housing and turned off by triple-tapping. These functions are enabled by an accelerometer, which also enables the Auto On feature, detecting the “raise to wake” motion. Other controls can be accessed via the Nucleus Smart App on iOS and Android devices or the optional CR310 remote control.

5.1.2 CP1150 Sound Processor Accessories

5.1.2.1 CP1150 Programming Adaptor Cable

The programming adaptor cable (Figure 6) enables the Sound Processors to be programmed via a connection to either a Cochlear Wired Programming Pod or Cochlear Wireless Programming Pod interface.

The programming adaptor cable connects the Sound Processors directly to the PIF5.2 programming interface. Connection to the PIF4 interface is enabled by connecting the CP1150 programming adaptor cable to the CP1000 Programming Cable.

Figure 6: Kanso 2 (CP1150) programming adaptor cable

5.1.3 Additional Components

5.1.3.1 Compatible implants

The CP1150 Sound Processor must be used together with a compatible implanted receiver-stimulator for normal operation. It is compatible with all CIC3 based implants and CIC4 based implants available in the market as listed below (Table 1). The CP1150 is not currently compatible with Nucleus 22 Series implants.

Table 1 Internal implants compatible with the Kanso 2 NF Sound Processors

Family	Model	Electrode
CI600 (CIC4)	CI612	Contour Advance
	CI622	Slim Straight Half Band Electrode
	CI624[1]	Slim 20
	CI632	Slim Modiolar Electrode
CI500 (CIC4)	CI512	Contour Advance
	CI513	Contour LEAP
	CI522	Slim Straight Half Band Electrode
	CI532	Slim Modiolar Electrode
	CI551[2]	Double Array
	ABI541	ABI
CI24RE (CIC4)	CI24RE(CA)	Contour Advance
	CI24RE(ST)	Straight
	CI24REH	Hybrid L24
	CI24RES	Hybrid S8, Hybrid S12
	CI24RE(CS)	Contour Straight
	CI422	Slim Straight Half Band Electrode
Nucleus 24 (CIC3)	CI24R(CS)	Contour
	CI24R(CA)	Contour Advance
	CI24R(ST)	Straight
	CI24M	Straight
	ABI24M	ABI
	CI11+11+2M	Double Array
	CI24MH (CI6+16+2M)	Hybrid

[1]not yet approved; [2]not commercially available in Europe

5.1.3.2 CR310 Remote control

The CR310 Remote Control allows the user to perform basic control functions on the paired Sound Processor, including changing programs, adjusting loudness and selecting the audio source. The Remote Control supports data communication via the NEO-XS Proximity 2 protocol over a 2.4 GHz wireless link and is compatible with the Kanso 2 NF Sound Processors.

5.1.3.3 Programming interfaces

The Kanso 2 NF Sound Processor is compatible with the Cochlear Wired Programming Pod and the Cochlear Wireless Programming Pod.

The Kanso 2 NF Sound Processor is compatible with Custom Sound 6.1 or later, which operates on a computer running Windows OS. It is not compatible with Nucleus Fitting Software (NFS) or Custom Sound Electric Potential.

5.2 Identity and Description of the Comparator

Kanso 2 (CP1150) Sound Processor:

Kanso (CP1150) Sound Processor is the commercially available predecessor device to the investigational Kanso 2 NF Sound Processor. Kanso 2 will be used as the comparator device for speech perception testing in quiet (CNC words) for both the NF and FF comparisons.

Nucleus 8 (CP1110) Sound Processor:

Nucleus 8 is an unapproved BTE Sound Processor. The Nucleus 8 is considered a suitable comparator for the OTE vs BTE comparison (secondary endpoint 2) because of the similarities to the commercially available predicate Nucleus 7 Sound Processor, and because Nucleus 8 includes signal processing features aligned with the next generation of OTE Sound Processor.

Table 2. Comparator conditions

Comparator	Endpoint	Justification
Kanso 2 (CP1150) Sound Processor	**Primary Endpoints** Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 Sound Processor and Kanso 2 NF Sound Processor	**Input processing:** Standard microphone directionality + SNR-NR + subject's own MAP and ADRO/ASC preference Standard microphone directionality has been chosen to be consistent with the microphone directionality that SCAN+ selects in a quiet setting, and because the impact of the notch filters have the greatest potential for impact on speech in quiet.
Kanso 2 (CP1150) Sound Processor	**Secondary Endpoints** Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 Sound Processor and Kanso 2 Sound Processor with FF	**Input processing:** Standard microphone directionality + SNR-NR + subject's own MAP and Adaptive Dynamic Range Optimisation Autosensitivity (ADRO/ASC) preference Standard microphone directionality has been chosen to be consistent with the microphone directionality that SCAN+ selects in a quiet setting, and because the research question includes the performance of FF in a quiet scenario.
Nucleus 8 (CP1110) Sound Processor	**Secondary Endpoints** Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 Sound Processor and Nucleus 8 Sound Processor	**Input processing:** Standard microphone directionality + SNR-NR + subject's own MAP and ADRO/ASC preference Standard microphone directionality has been chosen to be consistent with the microphone directionality that SCAN+ selects in a quiet setting
Kanso 2	**Exploratory Endpoint** Paired difference in percentage phonemes correct in quiet (50 dB) with the Kanso 2 Sound Processor and Kanso 2 NF Sound Processor NF	See primary endpoint justification

5.3 Accessory Device Requirements

Nucleus 8 Sound Processor

The Nucleus 8 SP must be used together with an implanted receiver-stimulator to achieve normal operation in clinical use.

To utilise the Sound Processor system, in addition to the processing unit, recipients will also use a compatible ear hook, battery module, coil, and magnet.

The Nucleus 8 Sound Processor is compatible with the Cochlear™ Wired Programming Pod.

Kanso 2 and Kanso 2 NF Sound Processors

The Kanso 2 Sound Processor and the Kanso 2 NF Sound Processor must be used together with an implanted receiver-stimulator to achieve normal operation in clinical use. The Kanso 2 Sound Processor and Kanso 2 NF Sound Processors NF are not currently compatible with the Nucleus 22 Series implants. For the current study, the implants in Table 2 will be used.

All study Sound Processors will be compatible with the Custom Sound Pro fitting software. This software will be used by the investigator to program the Sound Processors.

The research signal processing configurations will be programmed via CDI-Tool Version 7.3.1.

6 OBJECTIVES

6.1 Primary Objective

To evaluate the impact of NF on adult cochlear implant recipient's speech perception in quiet using an off-the-ear (OTE) Sound Processor.

6.2 Secondary Objectives

- To evaluate the performance of FF combined with standard microphone directionality on adult cochlear implant recipient's speech perception in quiet using an OTE Sound Processor.
- To compare adult cochlear implant recipient's speech perception in quiet with Kanso 2 and Nucleus 8 Sound Processors

6.3 Exploratory Objective

To characterise the impact of NF on adult cochlear implant receipients, phoneme perception in quiet using an OTE (Kanso 2) Sound Processor.

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

This is a pre-marketing, prospective, single-site, open-label, within-subject, pilot, interventional clinical investigation in adults with sensorineural hearing impairment who are current users of a Nucleus Cochlear Implant system.

See section 7.2 for description of subject population.

After enrolment, subjects will attend a single study visit as described in the CIP Schedule of Events (Section 3). At the study visit, 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.

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 subjects with repeated measures for each of the sound processing conditions to be evaluated. There will be two test sessions with no take home use between sessions. The test sessions will include words in quiet tests. 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 because the Kanso 2, Kanso 2 NF and Kanso 2 FF Sound Processors are physically identical, it may also be possible to conceal which Sound Processor is being used during testing.

Counterbalancing of the test order will be undertaken where possible to limit the influence of order effects on results.

7.2 Subjects

The subjects include men and women aged 18 years or older who are current users of a Nucleus 6 (CP910/920), Kanso 2 (CP1150), Kanso (CP950) or Nucleus 7 (CP1000) Sound Processor. Subjects will be screened, and 20 eligible subjects will be recruited to the clinical investigation. For speech perception testing, all subjects will receive all treatment and control conditions; however, the test order will be counterbalanced to control for order effects.

Written, informed consent must be obtained from the subject before any study procedures are initiated.

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, CI500 Series or Freedom Series
4) At least 6 months experience with a cochlear implant.

5) At least 3 months experience with a Nucleus 6 (CP910/920), Kanso (CP950), Kanso 2 (CP1150), or Nucleus 7 (CP1000) Sound Processor
6) MAP Total Stimulation Rate of 7.2kHz or greater
7) Able to score 30% or more with CI alone on a monosyllabic word in quiet test
8) Willingness to participate in and to comply with all requirements of the protocol
9) Fluent speaker in English as determined by the investigator
10) 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) Implant location that would result in undesirable hearing performance or discomfort with an off-the-ear Sound Processor, as determined by the investigator.
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 unless (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) Implanted with other active implantable medical devices (e.g., pacemaker, defibrillator).

7.2.3 Number of Subjects Required

The total number of subjects to be enrolled in the study to meet sample size calculation requirements is 12, which includes 3 additional subjects to account for an expected dropout rate of 25%.

7.2.4 Vulnerable Populations

Pregnant and breastfeeding women have not been excluded from this low-risk study. The are no benefits associated for pregnant and breastfeeding women to participate but there also no risks identified if they were to participate. It is to be noted that whilst we are not excluding pregnant or breastfeeding women, we are also not targeting them either.

7.2.5 Recruitment and Study Duration

The following subject status definitions apply:

- Enrolled: A subject that has a signed the Informed Consent form for the study.
- Screen Fail: An Enrolled subject that has been determined to not meet one or more eligibility criteria.

- Participated: Subjects who have met eligibility criteria and have commenced 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 complete the required treatment and visit schedule.

The recruitment period for the clinical investigation is estimated to be 4 weeks 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 3 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. 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
- Other (specify)

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

No treatment randomisation is planned. However, to control for order effects during speech perception testing for the Primary and Secondary Endpoints a 4x4 balanced Latin square order will be implemented (see table 3).

Table 3. Order of Administration of the Speech Perception Tests

	First Sound Processor	Second Sound Processor	Third Sound Processor	Fourth Sound Processor
SYD01, 05, 09	Kanso 2	Kanso 2 NF	Nucleus 8	Kanso 2 + FF
SYD02, 06, 10	Kanso 2 NF	Kanso 2 + FF	Kanso 2	Nucleus 8
SYD03, 07, 11	Kanso 2 + FF	Nucleus 8	Kanso 2 NF	Kanso 2
SYD04, 08, 12	Nucleus 8	Kanso 2	Kanso 2 + FF	Kanso 2 NF

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 as outlined in section 7.2.7 will be used to ensure that there is a balanced order or test conditions.

7.2.8 Post-investigation Medical Care

At the end of the study, subjects will return all investigational devices to the investigator and return to their own hearing devices. 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

Speech perception in quiet

Speech perception in quiet will be measured using the CNC monosyllabic words at 50 dB from S0 (zero degrees azimuth) position. There will be 2 lists per treatment or control (see Table 4 for Input processing conditions). The goal of speech perception assessment in quiet is to compare percent words and phonemes correct for each of the sound processing combinations.

Participant Evaluations and Procedures

Screening Visit

Included in this period:

- Written informed consent
- Eligibility including sentence in babble test if required
- Case Report Form Completion

Informed consent

See Section 10

Screening

Study investigators will screen each patient according to the inclusion and exclusion criteria. For subjects without relevant speech perception data on file, a words in quiet test will be conducted at 50 dB SPL. A score of 30% or more in the CI alone condition is required to pass that specific inclusion criteria. Subjects will be tested with their own sound processor and their own preferred signal processing settings for quiet environments.

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. 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 between the 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)
- 1 list of 50 words

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

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

Case Report Form

Once enrolled, the investigators will complete the following CRFs for each study subject.

- Demographics
- Medical history
- Hearing history
- Device history

Visit 1

Included in this period:

- Device Fitting
- Speech perception in quiet testing
- Case Report Form Completion

Device Fitting

Prior to assessing speech perception in quiet, the test Sound Processors will be loaded according to the input processing settings identified in Table 4.

ADRO is the adaptive dynamic range optimisation processing setting, and ASC is the auto sensitivity processing setting, both of which will be enabled or disabled in the test Sound Processors according to each subject's preferred settings on their own MAP; if the study subject uses and prefers ADRO and ASC in their own Sound Processor, then these setting will be enabled in the study Sound Processor.

SNR-NR is a single channel noise reduction algorithm and directionality refers to the microphone directionality that will be enabled. These signal processing settings will be enabled/disabled via the fitting software CDI Tool and Custom Sound Pro.

Speech perception in quiet test

In booth speech perception testing will be conducted using the input processing combinations and hardware listed in Table 4. The order of testing will be conducted according to the counterbalancing outlined in Section **Error! Reference source not found.**.

Table 4. Speech in Quiet test conditions.

	Notch filters	WNR	SNR-NR	Directionality	ADRO & ASC	FF
Kanso 2		✓	✓	Std	As per user preference	
Kanso 2 NF	✓	✓	✓	Std	As per user preference	
Nucleus 8		✓	✓	Std	As per user preference	
Kanso 2 FF		✓	✓	Std	As per user preference	✓(Mild)

Wind Noise Reduction (WNR); Signal to Noise Ratio- Noise Reduction (SNR-NR); adaptive dynamic range optimisa ion (ADRO); auto sensi ivity (ASC); ForwardFocus (FF)

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 between the 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.

Case Report Form

- Concomitant medications/therapies
- Adverse events
- Device deficiencies
- Device exposure

End of visit and return of study devices

Included in this period:

- End of study and return devices

After the speech perception evaluation has been completed, study subjects will return the study devices and will use their own device as normal in their home environment in between speech evaluation study visits.

Adaptive procedure:

Although no product changes are expected during the study period, early product can be sensitive to the low-risk issues identified in

Table 1. During this feasibility study these product issues may be identified by study subjects during the acute 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 5 identifies how issues will be investigated and retested by the research subjects.

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 study will be paused for all 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 1. 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 investigational 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.

7.4 Safety Evaluations and Procedures

The risks and anticipated ADEs for the Kanso 2 and Kanso 2 NF Sound Processor, as identified in Sections 8.2 and 8.3 of the CIP, will be assessed in the clinical investigation via reporting of all AEs/ADEs from the time of first subject first visit until last subject last visit.

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

7.4.1 Concomitant Medication and Therapies

There is potential that concomitant medical treatments may influence the outcomes of this study. 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 Speech Perception

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

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.

7.6 Sponsor Role in Conduct of the Clinical Investigation

Sponsor and investigator roles are assumed by Cochlear employees.

Cochlear has designed and will execute this clinical trial in-house at Cochlear Limited, Sydney. The study site 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 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.

8 Risks and Benefits of the Investigational Medical Device and Clinical Investigation

8.1 Anticipated Clinical Benefits

Study subjects will be asked to use hearing performance features on the Kanso 2 and Nucleus 8 Sound Processors during acute testing sessions, however this is not anticipated to provide benefits to the subject due to the acute nature of the testing.

Subjects who haven't previously experienced using the ForwardFocus feature may experience benefit of improved communication through reduction of distracting noise while using the feature during the acute test session only.

Due to the limited use of the investigational devices, there are no long-term clinical benefits anticipated for the study subjects.

8.2 Anticipated Adverse Device Effects

Cochlear's internal hazards analysis considers hazardous situations associated with the use of the Kanso 2 and Nucleus 8 Sound Processors (including internal battery) and Accessories. This hazards analysis considered basic safety, normal function, and reasonably foreseeable misuse, systematic or single fault conditions experienced by the user, operator or bystanders and environment.

The risks associated with the Kanso 2 and Nucleus 8 Sound Processors 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 8 Sound Processor such as pain or discomfort when wearing the processor and a risk that some sounds could be uncomfortable.

The following residual risks are disclosed in the Kanso 2 user guide:

- Small parts hazards.
- Suffocation hazard.
- Risk of high skin contact temperatures.
- Risk of high skin contact pressures.

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 programs on the Kanso 2, Kanso 2 NF and Nucleus 8 Sound Processors may sound different to each user's own Sound Processor; this is unlikely if study subjects enter the study already using a Nucleus 7 or Kanso 2 Sound Processor and more likely if they enter a study with a legacy device. 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.

Warnings and contraindications

See the Nucleus 7 and Kanso 2 Sound Processors User Guide for all Warnings and Contraindications. (user guides can be found within the 'Support' section of the country specific Cochlear website; www.cochlear.com). At this preliminary stage in development, the Nucleus 7 Sound Processor User Guide will be relevant for Nucleus 8 Sound Processor.

8.4 Risk Mitigation

The study investigational devices have been fully tested for safety, and the performance and use of the investigational devices is expected to be similar to the approved Nucleus 7 and Kanso 2 Sound Processors. 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; investigational procedures.

The residual risks related to the investigational device or procedure will be controlled in the following ways:

- The fitting and use of the Sound Processors will be supervised by the investigator. Test units will be used for a short duration (up to 3 hours) and will be used by adults who are able to indicate discomfort and remove the Sound Processor from their head.
- If recipients 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 Processors.
- Dropped devices should be inspected for external damage before re-use, to ensure there are no sharp edges/corners or rough surfaces.

8.5 Risk-to-Benefit Rationale

Residual risk levels associated with the Nucleus 8 and Kanso 2 Sound Processors (including the Kanso 2 NF Sound Processor) and Accessories have been determined to be as low as possible when the Sound Processor is used with a compatible cochlear implant and the programming adaptor cable. Based on pre-clinical testing of the Kanso 2 and Nucleus 8 Sound Processors along with a review of clinical investigations and published data on the Kanso 2 and Nucleus 7 Sound Processors, 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

For general statistical methods for reporting, details on the analysis populations, type-I error control, methods for handling missing data, criteria for the termination of the clinical investigation and procedures for reporting any deviations are described below.

9.2 Endpoints

9.2.1 Primary Endpoint

Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 NF and Kanso 2 (CP1150) Sound Processors

9.2.2 Secondary Endpoints

- Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 FF (standard omni) and Kanso 2 (standard omni) Sound Processors
- Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 and Nucleus 8 Sound Processor.

9.2.3 Exploratory Endpoints

Paired difference in percentage phonemes correct in quiet (50 dB) with the Kanso 2 NF and Kanso 2 Sound Processors

9.3 Hypotheses

For the non-inferiority test of CNCword score, the 95% CI (alpha=0.025 one-sided) for the mean paired difference (Kanso 2 NF versus Kanso 2 for the primary endpoint, Kanso 2 (no notch filters) + ForwardFocus (standard omni) versus Kanso 2 (no notch filters and standard omni) and Kanso 2 (no notch filters) versus Nucleus 8, respectively for the secondary endpoints) will be estimated. If the lower limit of the 95% CI of the mean paired difference is above -10%, 'Nucleus 8 SP' is regarded as non-inferior to 'Nucleus 7 SP' on that measure.

9.3.1 Primary Hypothesis

Endpoint: Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 (notch filters) and Kanso 2 (no notch filters) Sound Processors; higher score corresponds with a better outcome.

H0: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 NF Sound Processor (treatment) are inferior to those with the Kanso 2 Sound Processor (control)

Kanso 2 NF – Kanso 2 $\leq$ -10%

H1: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 NF Sound Processor (treatment) are non-inferior to those with the Kanso 2 Sound Processor SNR-NR on (control)

Kanso 2 NF – Kanso 2 > -10%

9.3.2 Secondary Hypothesis

Endpoint: Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 + FF (standard omni) and Kanso 2 (standard omni) Sound Processors

H0: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 FF Sound Processor (standard omni) (treatment) are inferior to those with the Kanso 2 Sound Processor (standard omni) (control)

Kanso 2 FF – Kanso 2 $\leq$ -10%

H1: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 FF Sound Processor (treatment) are non-inferior to those with the Kanso 2 Sound Processor (standard omni) (control)

Kanso 2 FF – Kanso 2 > -10%

Endpoint: Paired difference in percentage CNC Words correct in quiet (50 dB) with the Kanso 2 and Nucleus 8 Sound Processors

H0: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 sound processor (treatment) are inferior to those with the Nucleus 8 Sound Processor (control)

Kanso 2 – Nucleus 8 $\leq$ -10%

H1: Words in quiet (50 dB CNC words) scores (% words correct) with the Kanso 2 sound processor (treatment) are non-inferior to those with the Nucleus 8 Sound Processor SNR-NR on (control)

Kanso 2 – Nucleus 8> -10%

9.3.3 Exploratory Hypothesis

There are no exploratory hypotheses.

9.4 Sample Size Determination

This study is a non-inferiority design, and sample size calculation was based on non-inferiority tests for CNC word scores. The sample size using a confidence interval method (two-tailed 95% confidence interval) was estimated to have a reasonable power to detect non-inferiority word scores for the listed hypotheses.

To reject the null hypothesis of inferior word perception in quiet for the New processor:

- A margin of non-inferiority of 10% (new-old) has been chosen. That is saying that a true mean difference of anything up to 10% is acceptable and not clinically meaningful. This margin is based on clinical consensus, and previous feedback from the FDA
- An expected standard deviation of difference scores of 7.5% for CNC words (50 dB), based on previous OTE studies investigating words in quiet.
- A significance level $\alpha = 0.05$ (two-tailed).
- A desired power of 0.9.

Based on these assumptions, a sample size of 9 subjects is required to reject the null hypothesis. An increased sample size of 12 subjects will be enrolled, which will allow for the possibility that the variability in difference scores will be greater than expected and to account for the possibility of subject attrition.

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 measurement 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:

Words in quiet scores at different speech testing conditions will be listed and summarised descriptively by treatment group and study population. Figures as appropriate to further describe the data may be presented.

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.

If non-inferiority is demonstrated, the testing will proceed to a test of superiority.

9.7 Secondary Endpoint Analyses

See section 9.6

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

Not applicable

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 Nucleus 8 SP Hazards Analysis.

NOTE: An anticipated serious adverse device effect is an effect, which by its nature, incidence, severity, or outcome has been identified in the Nucleus 8 SP Hazards Analysis.

11.1.6 Adverse Events of Special Interest

Not applicable.

11.1.7 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.

AEs will be recorded from the time of first use of the IMD. AE recording will continue for each subject until completion of their End of Study visit. Ongoing SAEs and 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's 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 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;

a) suitable action had not been taken,

b) intervention had not been made, or,

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 24 hours.

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

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

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

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

11.4.2 Sponsor Notification of Events

The Sponsor is responsible for reviewing all safety data to evaluate potential causality and anticipation of all ADEs.

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 contact person of the Sponsor:	Clinical Review Board
Country and time zone:	Australia, Australian Eastern Standard Time
Email:	[redacted]

11.5 Independent Data Monitoring Committee

Not applicable.

12 Device Accountability

Supply of all 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.

Contact information regarding the IMD 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 7 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 15 years after completion of the investigation or after the last device was placed on the market, if the IMD has market authorisation.

The Sponsor will notify the Principal Investigator when records are no longer needed. The Investigator will not discard any records without notifying the Sponsor. If the Principal Investigator moves from the current investigational site, the Sponsor should be notified of the name of the person who will assume responsibility for maintenance of the records at the investigational site or the new address at which the records will be stored. The Investigator will notify the Sponsor as soon as possible in the event of accidental loss or destruction of any study documentation.

20 Publication Policy

This clinical investigation will be prospectively registered at clinicaltrials.gov.

No joint peer-reviewed publication is planned from this study.

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 site qualification, initiation, monitoring, and close out.

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

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

Peterson GE, Lehiste I. Revised CNC lists for auditory tests. J Speech Hear Disord. 1962;27(February):62-70. doi:10.1044/jshd.2701.62

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	Change has been made to the standard exclusion criteria: From: Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device. To: Currently participating, or participated in another interventional clinical study/trial in the past 30 days unless (if less than 30 days) the prior investigation was Cochlear sponsored and determined by the investigator to not impact clinical findings of this investigation.	Cochlear sponsored trials looking at sound processors and signal processing are not treating life-threatening illnesses, they are low risk and low intensity for the patient. The potential confounding effect of a Cochlear investigational device is understood and there is no expected washout period expected. There is no need for patients to enrol without a 30-day break if the previous trial was a Cochlear sponsored trial.
	Pregnant or breastfeeding women have not been excluded from study.	This is a low-risk and non-invasive study.
	Change has been made to the Safety Evaluations and Procedures: From: Safety data adjudication may be conducted by the Sponsor's Medical Officer in accordance with the Sponsor's standard operating procedures. To: Safety data adjudication will be conducted by the Sponsor's Clinical Review Board in accordance with the Sponsor's standard operating procedures	Business process change

APPENDIX 1: STATEMENT/DECLARATION OF DEVICE CONFORMITY

Clinical Investigation Details:

Clinical Investigation ID:	CLTD5818
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:	Kanso 2 Notch Filter (NF) Sound Processor Kanso 2 with Forward Focus (FF) CDI Tool Version 7.3.1 Nucleus 8 (CP1110) Sound Processor

We, Cochlear Limited, declare that, where appropriate, technical and biological and pre-clinical evaluations have been conducted and, as a result, the investigational devices conform 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, Regulatory Affairs
Signature:	
Date:	

Signature Page for VV-TMF-08761 v1.0

Reason for signing: Approved	Name: [redacted] Role: A Date of signature: 01-Feb-2022 04:01:59 GMT+0000

Signature Page for VV-TMF-08761 v1.0