Clinical Investigation Plan

Investigation Title: A feasibility, prospective, repeated-measures investigation to investigate innovations in clinical care in adult and paediatric recipients implanted with CE approved Nucleus cochlear implants: an umbrella investigation.

Short Title:	**Clinical Care**
CIP Number:	**AI5763**
Date:	**Refer to Header**
Sponsor	**Cochlear Limited** **1 University Avenue** **Macquarie University NSW 2109** **Australia** **Phone: +61 294 28 65 55**

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: NCT05270876

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Sponsor Organisations	Cochlear Limited 1 University Avenue Macquarie University NSW 2109 Australia Phone: +61 294 28 65 55
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Clinical Research Organisation	Belgium: TRIUM Clinical Consulting Baron Opsomerlaan 32 2500 Lier, Belgium Australia: Avania Pty Limited 13/76 Reserve Road, Artarmon NSW 2064
Safety Contact	CLTD-SafetyMonitor@cochlear.com

A complete list of participating Principal Investigators' names, titles and addresses, and the names and addresses of participating institutions (sites) will be maintained by the Sponsor and will be provided as a separate Principal Investigator List. The definitive Principal Investigator list will be provided in the Clinical Investigation Report.

INVESTIGATOR AGREEMENT

Coordinating 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]	Coordinating Investigator
Signature	**Date**

Principal Investigator Declaration

By my signature below, I confirm that I have read, understood and will strictly adhere to the requirements therein. I undertake to ensure that all staff with delegated responsibilities in the conduct of this CIP have also 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**
	Principal Investigator
Site Name	**Site Address**
Signature	**Date**

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1 DEFINITIONS AND ABBREVIATIONS

Term	Description
ADE	Adverse Device Effect
AE	Adverse Event
BTE	Behind-The-Ear processor
CI	Cochlear Implant
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CIRA	Clinical Investigation Research Agreement
CRF	Case Report Form
CSS	Custom Sound Suite
CTC	Cochlear Technology Centre Belgium
DD	Device Deficiency
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GCP	Good Clinical Practices
IB	Investigator's Brochure
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
IDMC	Independent Data Monitoring Committee
IFU	Instruction For Use
IMD	Investigational Medical Device
NFS	Nucleus Fitting Software
NRT	Neural Response Telemetry
OTE	Off-The-Ear processor
Pod	Programming interface
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SOP	Standard Operating Procedures
SP	Sound Processor
USADE	Unanticipated Serious Adverse Device Effect

2 CLINICAL INVESTIGATION SYNOPSIS

Investigation title	A feasibility, prospective, repeated-measures investigation to investigate innovations in clinical care in adult and paediatric recipients implanted with CE approved Nucleus cochlear implants: an umbrella investigation.
Short title	Clinical Care
Investigation number	AI5763
Name of investigational medical device(s)	New/improved fitting, diagnostic and (re)habilitation software and/or research tools/methods.
Intended use of investigational medical device(s)	Exclusively used for feasibility study only. Pre-market.
Name and description of comparator device/product(s)	Commercially available fitting, diagnostic and (re)habilitation software and/or tool/method where available.
Estimated recruitment period	Up to 4 years and 10 months (October 2024).
Expected duration per subject	Up to 5 years.
Number of subjects planned	Maximum 160 subjects enrolled in a collection of feasibility sub-studies. Belgium: Adults and children Australia: Adults only
Number of investigational sites planned	5
Inclusion criteria	• Group 1 subjects: Users of a CE approved Nucleus cochlear implant, resulting in open set speech understanding or Group 2 subjects: Subjects assessed by their CI clinic to be suitable for implantation with a commercially available CE approved Nucleus cochlear implant. • Paediatrics: Older than 10 months and <18 years when entering the study (Belgium only) or Adults: ≥18 years when entering the study (Belgium and Australia). • Subject/legally designated representative is fluent speaker in the language used for assessments. • Willing and able to provide written informed consent (for paediatric populations this criterion applies to the parent/legally designated representative).
Exclusion criteria	• Unable or unwilling to comply with the requirements of the clinical investigation as determined by the investigator. • Additional health factors, known to the investigator, that would prevent or restrict participation in the audiological evaluations. • Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.

	• Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of this investigation. • Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device.
Primary Objectives	• To evaluate the effectiveness of new streamlined and optimized device fitting methods.
Secondary Objectives	• To evaluate the effectiveness of new diagnostic and outcome prediction methods. • To evaluate the effectiveness of new training and counseling schemes for hearing implant users. • To evaluate the usability of the new fitting, diagnostic methods and training/counseling methods from the recipient and/or the clinician's point of view.
Primary Endpoint	• Monosyllabic word in quiet scores (for standard-of-care and new/optimized device fitting methods)

3 SCHEDULE OF EVENTS

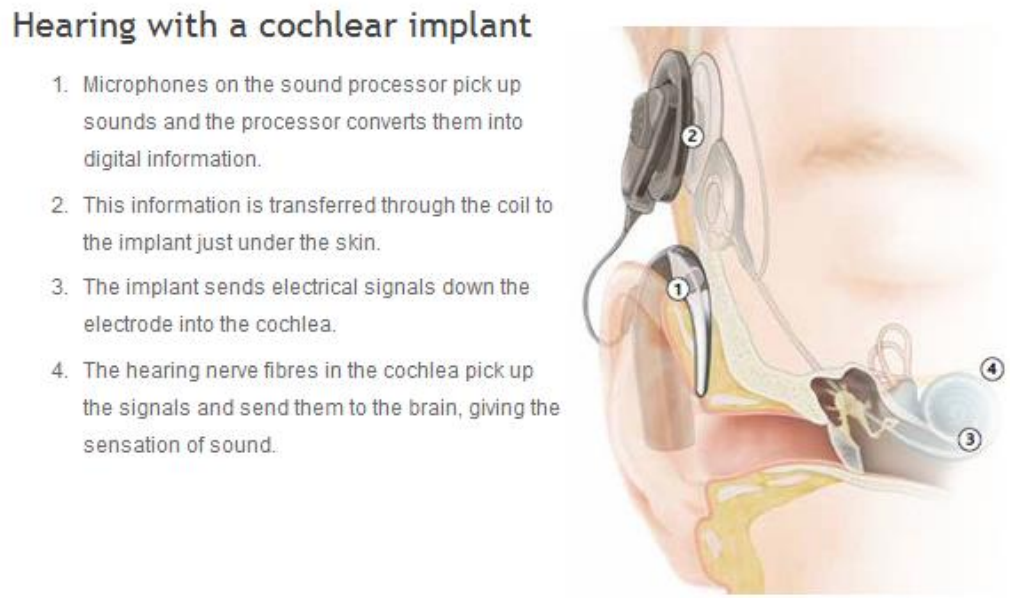
The specific procedure of each sub-study will be described in the study documentation of the sub-study.

4 BACKGROUND INFORMATION AND RATIONALE

4.1 Introduction

Cochlear implants (CI) are electronic devices for adults and children who do not receive adequate benefit from conventional hearing aids. The cochlear implant system consists of an internal implant and an externally worn sound processor (SP). The microphone of the sound processor picks up the sound and turns it into a digital encoded signal. The sound processor transmits this digitally coded signal through the coil to the implant. The implant converts this signal into electrical pulses and sends them along the electrode array placed in the cochlea. The electrodes of the implant then stimulate the cochlea's hearing nerve (Figure 1).

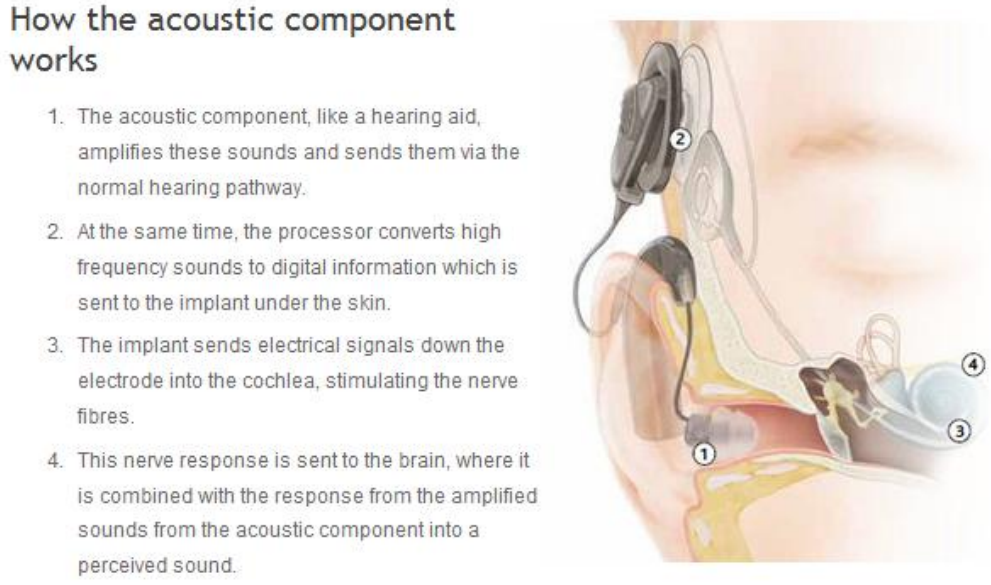
Figure 1 Nucleus cochlear system: electrical hearing



For those recipients who have severe to profound high frequency hearing loss but who maintain useful low frequency hearing in the implanted ear, acoustic hearing can be added to the electrical hearing path (electro-acoustic stimulation/Hybrid). An acoustic component is attached to the sound processor, thereby delivering acoustic amplification in a similar way to a conventional hearing aid (Figure 2).

In case the recipient has residual hearing in the contralateral ear, a standard hearing aid can be used in the non-implanted ear.

Figure 2 Nucleus cochlear system with acoustic component: electro-acoustic hearing



Programming of the sound processor is in general done by an expert clinician using clinical programming software. Clinicians also perform performance measurements to assist in the programming and management of the CI recipient. The programming and performance measurements are very time-consuming tasks for specialised clinics. Moreover, clinical models around the world are very different and are evolving rapidly. Therefore, there is a strong tendency to look for less time consuming and specialised methods to reach the same goal, namely optimal hearing for the user.

Hearing loss is a chronic condition, requiring acute but also long-term care. Due to the technological evolution, in the coming years the devices may have an in-built wireless connection to the internet. Users, including elderly people, are becoming fluent users of mobile and computer devices. Therefore, new hearing care models can be developed. Four different models can be identified:

(1) expert care where the hearing implant user travels to the CI clinic to meet with expert clinicians, specialized in hearing implants.

(2) local care where the hearing implant user can personally meet with a (less specialized) hearing professional offering certain services in the local neighbourhood.

(3) remote care where the implant user can contact professional care providers from home through internet and mobile technologies at a time convenient for both parties; and

(4) self-care where the implant user has access to certain aspects of care (e.g. counselling materials, self-test tools, self-fitting tools, objective datalogs, rehab materials, web shop, …) through internet technologies at any time.

New technologies need to be investigated to accommodate these 4 models.

This investigation evaluates these new technologies for the complete hearing journey from the recipient and the clinician's perspectives on the different aspects of device fitting, diagnostics, performance and rehabilitation methods for the four models of care.

Firstly, new fitting technologies and methodologies focus on the work flow and the tools to optimally and efficiently program a cochlear implant, be it purely electrical hearing, or a combination of electrical and acoustical hearing.

Secondly this study evaluates the hearing performance and outcomes a user obtains (through e.g. audiological tests and questionnaires) as well as the diagnostics in case of degrading performance. This includes classic audiological measures such as tonal audiometry and speech understanding, but also covers psychoacoustical and objective assessments, cognitive function evaluation etc. These measures are used in building predictive models for an individual. A last aspect of diagnostics is monitoring hearing performance and the long-term use of the device. Devices must become more intelligent and pro-active in reporting problems (e.g. using data logging) and suggesting solutions.

A well-fitted hearing implant is a necessary condition for the user to reach his/her full hearing potential. This goes hand in hand with optimal training and rehabilitation a user must go through with their new hearing modality. Therefore, the effectiveness of new training and counselling schemes for the users is also evaluated in this study.

The effectiveness of these different methods for fitting, diagnostics and (re)habilitation will be evaluated as well as the usability of each of them for both the cochlear implant recipient and/or parent/legally designated representative and the clinician.

The umbrella investigation will be conducted in different sub-studies to assess the incremental change of the software functionality and/or to assess the concept of a new diagnostic, fitting or (re)habilitation method. Each sub-study will be submitted separately with a sub-study specific Clinical Investigation Plan (CIP) and a sub-study specific Informed Consent Form (ICF). A status update will be reported yearly, and a close-out report will be provided at the end of the study. For each sub-study a Clinical Investigation Report (CIR) will be delivered. Since different methods will be tested, subjects may be recruited for multiple sub-studies or stages of the project. Each subject can only participate in one sub-study at a time. This is further described in section 7.

4.2 Findings of Previous Nonclinical and Clinical Studies

4.2.1 Nonclinical Data

Not applicable

4.2.2 Clinical Data

The existing methods are studied extensively, and many publications are available. Current literature on the sound processors is contained within the Investigator Brochures (IB) of the current commercially available sound processors.

A detailed description of clinical data for the sub-study will be described in the sub-study specific documentation.

4.3 Study Rationale

To evaluate the benefit of new features as mentioned in section 4.1, it is essential that studies are performed with a relevant group of human users (adults or paediatrics), that is, cochlear implant users (including electro-acoustic), either unilateral, bilateral and/or bimodal. The evaluation can be performed in the laboratory in an acute session or in real world environments with take-home device use to further validate their benefits. A sub-study specific rationale can be found in the sub-study specific documentation.

5 MEDICAL DEVICE INFORMATION

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

As mentioned in section 4.1, a cochlear implant system consists of the internal implant and the externally worn sound processor. This system also contains a remote control unit or an application on a mobile device (e.g. Nucleus Smart App). The external hardware is programmed using fitting software which downloads the firmware onto the sound processor. Different diagnostic and (re)habilitation applications are used to diagnose and optimize the performance and use of the cochlear implant system.

The hardware and software of the current generation Nucleus cochlear implant system are shown in Figure 3 and Figure 4. It is expected that these components will evolve over the next 5 years. However, the basic architecture will remain unchanged.

Essentially the following technological components are needed.

(1) An implantable receiver/stimulator is implanted in the mastoid with the electrode placed in the inner ear. In the hermetic titanium housing is a specialized electronics board that produces the electrical stimulation pattern that is delivered to the auditory nerve. The unit is specifically designed for stimulation of the auditory nerve (pulse strength, pulse waveform) and contains many in-built safety functions (capacitors blocking DC currents, current source strength limitations and continuous error checking, …).
(2) The sound processor is typically worn on the ear (i.e. behind-the-ear processor or BTE) or on the head (i.e. off-the-ear processor or OTE) and consists of an electronics board and a battery in a plastic housing. Its role is to capture the sound - typically from the in-built microphones but other inputs are supported as well – and to analyze the sound and calculate the corresponding electrical stimulation pulses and acoustic output (in case of electro-acoustic stimulation). These are sent as commands to the implantable receiver/stimulator through the wireless link. The hardware is designed in compliance with all applicable medical device standards for optimal wearing comfort.
(3) The firmware is the software running continuously on the sound processor. It determines the stimulation that will be provided. Many features have been added to the sound processing algorithms, such as noise reduction functions, directionality, sound environment classification, flexible audio sources and wireless connectivity, …. The firmware also contains various safety related functions, e.g. it stores the electrical stimulation levels that are comfortably loud for the specific patient etc.
(4) The fitting software is the software with which the clinician is programming the sound processor. It downloads the firmware onto the sound processor and determines the patient specific parameters, e.g. stimulation levels. The fitting software can run on computer, a tablet, or a mobile device allowing self-tuning.

(5) Diagnostic tools and (re)habilitation. Diagnostic tools can provide direct stimulation in order to measure an aspect of the auditory nerve response (e.g. neural response telemetry) in which case they replace the firmware on the sound processor. Or they can be audio based, playing special sounds, in which case this audio signals are processed in the standard way by the firmware. Rehabilitation tools (hearing and cognitive training) also fall under this latter category.

Figure 3 Hardware of the Nucleus Cochlear Implant System: internal implant, sound processor (OTE/BTE eventually with acoustic component), remote control/App on mobile device

This study will not investigate changes to the internal implant nor to the external hardware (i.e. SP and remote control). Only new technologies that become available in the fitting software, sound processor and remote control firmware/App, diagnostic and rehabilitation tools and applications, are investigated in this study.

Figure 4 Software: Programming Software (Custom Sound), [redacted] and electrophysiology software (CSEP)

The current commercially available fitting tools for Nucleus cochlear implants are Custom Sound [redacted] (CSS) and [redacted]. New fitting methodologies and tools will be implemented

either in a new build of the existing CSS and [redacted] software (if the modification to the standard functionality is small) or in Cochlear's research platforms.

Also, the new diagnostic and outcome prediction methods, as well as the new training and counselling methods that are under investigation, will use new software.

. Subjects will use the IMD for the duration of the sub-study only, and that device will be removed when each sub-study is concluded.

The specific manufacturer, build or version of each investigational component (software, firmware or application), will be logged and described in the procedures document of each sub-study. Statements of conformity for the investigational software and firmware will be provided in the sub-study documentation. For each investigational component there will be a test plan, test report and release report. The IMD and/or the packaging for the device will be clearly labelled to identify it as exclusively for use in a clinical investigation, as mentioned in section 12. Traceability of the build number will be documented in the tracking forms such as the Sponsor Device Tracking Form (1295388) and Software Tracking Form (1302326), as mentioned in section 12. The investigator will be trained on using the IMD. This training will be logged in a training log.

The investigational devices will not be in contact with body fluid or tissue.

5.2 Identity and Description of the Comparator

New fitting methodologies and tools will be investigated by using a new build of the existing CSS, [redacted] software and by other Cochlear's research platforms. This will be compared to the commercially available fitting methods and tools where available.

Also new diagnostic and outcome prediction methods, as well as new training and counselling methods, using new software and tools, will be compared to the currently available methods and tools.

A detailed description of the comparator will be described in the sub-study specific documentation.

5.3 Accessory Device Requirements

Not applicable

6 OBJECTIVES

The following objectives apply for umbrella study AI5763. A sub-study addresses aspects of one or more of these objectives and will be specified in the study documentation of that specific sub-study.

6.1 Primary Objectives

- To evaluate the effectiveness of new streamlined and optimized device fitting methods.

6.2 Secondary Objective

- To evaluate the effectiveness of new diagnostic and outcome prediction methods.

- To evaluate the effectiveness of new training and counseling schemes for hearing implant users.
- To evaluate the usability of the new fitting, diagnostic methods and training/counseling methods from the recipient and/or the clinician's point of view.

6.3 Exploratory Objective

There are no exploratory objectives stated in the umbrella investigation, however, they will be specified in the sub-study documentation if appropriate.

7 DESIGN OF THE CLINICAL INVESTIGATION

7.1 General

This is a feasibility, prospective, with sequential enrolment, multicenter, clinical investigation in adults and paediatrics with a CE approved Nucleus cochlear implant.

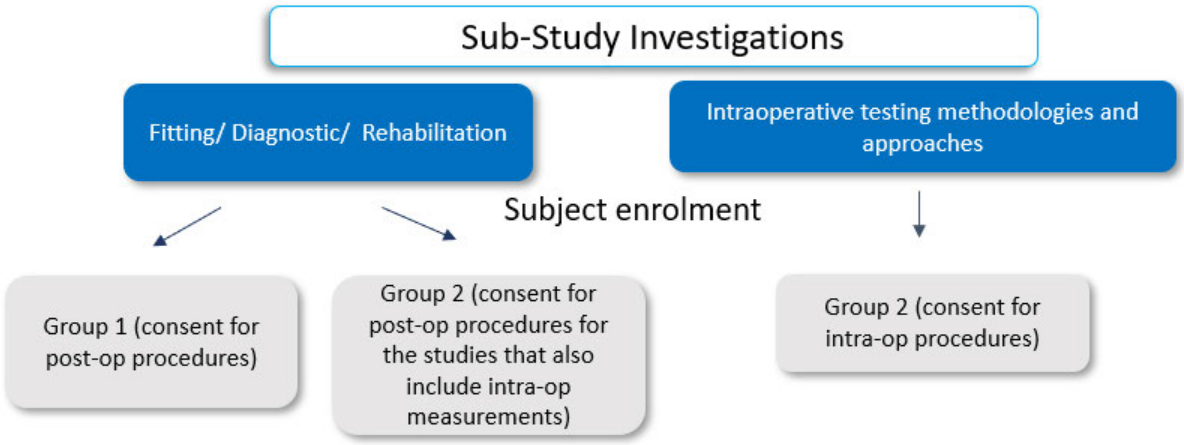
Subjects older than 10 months will be included. Subjects will be screened and up to 160 eligible subjects will be recruited in the umbrella investigation.

Two separate groups of subjects will be recruited:

- Group 1 will include subjects who are already implanted with a Nucleus cochlear implant. A clinical setting can consist of therapeutic elements (fitting, diagnostic or rehabilitation) and evaluations. Subjects will be assessed with the commercially available Nucleus sound processor. Acute testing will be done where possible. Take home use will be applied when learning effects may play a significant role and to evaluate the acceptance of the different fitting, diagnostic and (re)habilitation methods in as many listening environments as possible. The subject might be asked to complete questionnaires, to perform at-home tests etc. during this take home use and/or at the clinical visits. The time for a clinical visit will be limited to a maximum of 4 hours. The time in between clinical visits will vary with typical spacing of between 0 (acute) to 4 weeks.
- Group 2 will include subjects who are scheduled to be implanted with a commercially available Nucleus cochlear implant. The diagnostic testing will be conducted in the operating theatre during the cochlear implant surgery. Only CE approved devices will be used for this intra-operative testing in accordance with the approved indication(s) and terms of the market authorization. Post-operatively, these subjects might be recruited following the procedures as described for the group 1 subjects.

  Figure 5 illustrates the subject enrolment scenarios for group 1 and group 2 subjects.

Figure 5 subject enrolment scenarios for group 1 and group 2 subjects.



Subjects will attend scheduled study visits over a period up to 5 years in different sub-studies as described in the sub-study documentation.

A clinical setting can consist of therapeutic elements and evaluations. Subjects will be assessed with the commercially available Nucleus sound processor if required. Acute testing will be done where possible. Take home use will be applied when learning effects may play a significant role and to evaluate the acceptance of the new listening program, diagnostic or rehabilitation tool in as many listening environments and/or in daily life as possible. The subject might also be asked to complete questionnaires, to perform at-home tests etc. during this take home use and/or at the clinical visits. The time for a clinical visit will be limited to a maximum of 4 hours. The time in between clinical visits will vary with typical spacing of between 0 (acute) to 4 weeks.

The description of the measures taken to minimize bias, such as randomization and blinding, will be described in each sub-study specific documentation. Also, the sub-study specific method and timing for assessing, recording and analyzing variables, the equipment used, the monitoring maintenance and calibration will be described in the sub-study specific documentation.

Section 7.3 describes the procedure used in the umbrella investigation.

Safety will be assessed by recording and summarizing all Adverse events (AEs)/Adverse Device Effects (ADEs) and Device Deficiencies (DDs). Sub-study specific endpoints and details such as specific measurements and time points for assessment of each measure, will be described in each sub-study specific study documentation. No Independent Data Monitoring Committee (IDMC) will be used for this clinical investigation. Analyses, including interim analyses where required, will be specified in the sub-study CIP. All subjects will have an End-of-Study visit at the time they complete each sub-study and the umbrella study.

The specific study design of each sub-study will be described in the study documentation of the sub-study.

7.1.1 Design Rationale

The goals of this study are

- to measure hearing outcomes to assess performance and/or
- to obtain better diagnostics and/or
- to achieve higher convenience for implant users and hearing care professionals and/or
- to determine whether device and procedure improvements deliver an improvement in time efficiency for the CI recipient and the clinician involved in the CI process.

The outcomes of the study will guide Cochlear to select features for inclusion in future cochlear implant systems and/or future models of care.

This investigation can be divided in two stages, namely the intra-operative stage and the post-operative stage, during which evaluation will take place.

Post-operative stage to evaluate new fitting, diagnostic and (re)habilitation methods and tools

Multi-channel cochlear implants have been highly successful in restoring speech understanding to individuals with severe-to-profound hearing loss. Optimal programs are those programs (or parameter settings) that result in an optimal hearing outcome with the cochlear implant. Classic methods of cochlear implant programming involve measuring the lowest stimulation level at which the recipient is able to detect sound through the cochlear implant (threshold, or T- level) and also the highest stimulation level that provides a comfortable percept (comfort, or C- level) to the recipient. Such measurements are obtained on electrodes across the electrode array. This process can be time consuming and can produce varied results depending on the skill of the clinician and the responsiveness of the recipient. Performance measurements (e.g. audiological tests, questionnaires, quality ratings, etc.) and/or objective measurements (e.g. datalogging, impedances, neural response telemetry etc.) are also collected to assist in programming. At every stage in the cochlear implant process (re)habilitation is given to the CI recipient by dedicated professionals, self-care tools, online tools etc.

It is important to continually improve the efficacy of the methods to create programs and make performance assessments. The vast majority of the CI users can be considered as routine cases, where there are no specific medical complications (such as e.g. cochlear malformations or neuropathy etc.). For this group an overall streamlined process resulting in consistent high hearing outcomes can be achieved, even when programmed by clinicians with a range of clinical experience, professionals or potentially by recipients themselves. The same applies for a streamlining in the diagnostic and (re)habilitation methods.

Cochlear is developing such streamlined methodologies (Botros et al 2013, International Journal of audiology).

To optimally manage the more complex cases, it is important that the clinician still has access to detailed device control features (such as activation of individual electrodes). Specific diagnostic methods are also needed to identify the areas where the patient is encountering difficulties, e.g. through hearing tests or diagnostic tests. The clinician can then better decide how to change elements of the therapy.

Future clinical management methods should therefore combine device control functions and diagnostic tests. It is conceivable even that smart algorithms will be developed that will assist in changing the map parameters quasi-automatically. The aim of the programming and performance evaluation methods is to improve on average hearing outcomes while streamlining the process, improving the efficacy, and lowering the health care cost.

Incremental changes will be made to the research software used for programming, performance evaluations and rehabilitation so that the right balance of ease of use and efficacy is maintained.

Intra-operative stage to collect objective measurements

Objective measurements, for example Auto-NRT and impedance telemetry are commonly used test procedures to test the implant function intra- and post-operatively. These measurements utilise the capability of the internal implant to run telemetry tests when commanded by the sound processor. Currently these tests are run either via a computer with Custom Sound [redacted] software or with a remote control or App on a mobile device handled by the professional.

These objective data can be used in fitting and can eventually help the clinician with predicting outcomes, increase performance and optimise the clinicians' efficiency in diagnostics.

In this investigation, only CE approved devices will be used for this intra-operative testing in accordance with the approved indication(s) and terms of the market authorization. Post-operatively, these subjects might be recruited following the procedures as described for the group 1 subjects.

Comparison of programming, diagnostic and/or (re)habilitation methods is typically conducted using repeated-measures design, in which each subject is acting as his/her own control, which accommodates the heterogeneity across the population. The baseline condition will be compared to one or more of the investigational conditions.

As mentioned in section 4.1, this umbrella investigation will be conducted in different sub-studies to assess the incremental change of the software functionality and/or to assess the concept of a new diagnostic, fitting or (re)habilitation method. Each of the sub-studies will be looking at a particular approach to address the objectives of the overall umbrella investigation AI5763.

Since different methods will be tested, subjects may be recruited for multiple sub-studies, during the full duration of the umbrella investigation. Each subject can only participate in one sub-study at a time.

CI recipients from the age of 10 months upwards can participate in the study, as long as they meet the inclusion and exclusion criteria as described in section 7.2. Children are included in the study as they are a specific group of CI users, requiring adapted fitting, diagnostic and (re)habilitation methods compared to adult CI users. The procedure for recruiting subjects is further described in section 7.2.

Where possible, each sub-study will be blinded (i.e. information is concealed from the recipient) or double-blinded (i.e. information is concealed from the recipient and the investigator) and randomized (i.e. the order of testing).

Given that the sub-studies are feasibility studies, there is no need to statistically power the study. However, where possible sample size calculation will be made to enable assessment of non-inferiority or superiority. This is described in section 9.

7.2 Subjects

Written, informed consent must be obtained from the subject or subject's legally authorized representative before any study procedures are initiated.

Eligibility of subjects shall be supported by medical, demographics and audiological information that confirm the subject inclusion as stated in section 7.2.1.

Up to 160 adult and paediatric CI recipients older than 10 months can participate into the umbrella study. Each sub-study will specify their own subject population and indications for which the IMD is intended, within the population and indications of the umbrella investigations. Paediatric subjects will be enrolled in Belgium only

7.2.1 Inclusion Criteria

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

- Group 1 subjects: Users of a CE approved Nucleus cochlear implant, resulting in open set speech understanding or

  Group 2 subjects: Subjects assessed by their CI clinic to be suitable for implantation with a commercially available CE approved Nucleus cochlear implant.
- Paediatrics: Older than 10 months and <18 years when entering the study (Belgium only)
  or
  Adults: ≥18 years when entering the study (Belgium and Australia)
- Subject/legally designated representative is fluent speaker in the language used for assessments.
- Willing and able to provide written informed consent (for paediatric populations this criterion applies to the parent/legally designated representative).

7.2.2 Exclusion Criteria

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

- Unable or unwilling to comply with the requirements of the clinical investigation as determined by the investigator.
- Additional health factors, known to the investigator, that would prevent or restrict participation in the audiological evaluations.
- Investigator site personnel directly affiliated with this study and/or their immediate families; immediate family is defined as a spouse, parent, child, or sibling.
- Cochlear employees or employees of Contract Research Organizations or contractors engaged by Cochlear for the purposes of this investigation.
- Currently participating, or participated within the last 30 days, in another interventional clinical investigation/trial involving an investigational drug or device.

7.2.3 Number of Subjects Required

Up to 160 subjects will be included in this umbrella study. Most subjects will be unilateral adult users and additionally bilateral and bimodal users will be recruited. Also, paediatric subjects from the age of

10 months upwards (see section 7.2.4) could be recruited, but only when strictly required by a specific sub-study.

This umbrella study explores the feasibility phase of new or improved fitting, diagnostics and (re)habilitation methods or tools. No formal power calculations are performed on the level of the umbrella investigation. In case a sample size calculation is done for a specific sub-study, the total number of subjects to be recruited in the sub-study as well as the expected dropout rate will be described in the study documentation of the sub-study.

7.2.4 Vulnerable Populations

As described in previous sections, this umbrella study will evaluate the benefit of new features. Each method/tool will be evaluated in a sub-study. Depending on the specific aspect that will be tested, children might be involved from the age of 10 months upwards. The sub-study specific information will be given to the parents/ legally designated representative of the subject and will be adapted as well towards the cognitive level of the subject. The Informed Consent Form (ICF) will be signed by the parents and/or legally designated representative of the subject.

Paediatric subjects will be enrolled in Belgium only.

No extra medical care will need to be provided after the clinical investigation.

7.2.5 Recruitment and Study Duration

The following subject status definitions apply:

Enrolled: A subject that has a signed 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 all eligibility criteria and started on protocol defined procedures.

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.

The recruitment period for the clinical investigation is estimated to be 4 years and 10 months from the time of first subject consent to recruitment of the last subject. No new subjects will be recruited in the last 2 months of the study.

Each participant can participate in several sub-studies (one at a time).

Clinical Investigation completion is last subject last visit. In the event of ongoing Serious Adverse Events (SAEs)/Serious Adverse Device Effects (SADEs) at the time of this last visit, the clinical investigation completion will be extended for a further 30 days, or until resolution or stabilization of the event, whichever comes first. Any variations to these requirements will be documented in each sub-study documentation (for example, variations to account for in-booth only or take-home use).

7.2.6 Criteria for Subject Withdrawal

Subjects can decide to withdraw from the investigation at any time. 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

If subject withdrawal is due to problems related to the IMD and/or comparator safety or performance, the Investigator shall ask for the subject's permission to continue in safety follow up (i.e., adverse events) until their scheduled End-of-Study visit. Withdrawal from the umbrella investigation will also result in withdrawal from any active sub-study under this umbrella investigation.

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

Participating subjects who are withdrawn/discontinued might be replaced. This will be specified in the sub-study documentation.

7.2.7 Randomisation Procedures

Subjects who meet all eligibility criteria for participation may be randomised to an intervention based on a randomisation schedule prepared by the Sponsor. Any randomisation requirements (such as the storage and access of randomization codes) will be defined on a sub-study basis and defined in the sub-study documentation.

7.2.7.1 Blinding Procedures

Where possible, each sub-study will be blinded (i.e. information is concealed from the recipient) or double-blinded (i.e. information is concealed from the recipient and the investigator). When blinding will be used in a sub-study, the procedures of blinding and unblinding, the emergency situations for unblinding etc. will be described in the sub-study documentation.

7.2.8 Post-investigation Medical Care

No extra medical care needs to be provided after the clinical investigation.

7.3 Performance Evaluations and Procedures

The study is a multi-center study conducted at following sites:

Belgium:

External sites: GZA Sint-Augustinus Antwerp and AZ Sint-Jan Brugge-Oostende AV

Internal (Cochlear) site: Cochlear Technology Centre Belgium (CTC).

Australia:

External site: HEARnet (in collaboration with Royal Victorian Eye and Ear Hospital, East Melbourne)

Internal (Cochlear) site: Cochlear Ltd. Melbourne.

The principal investigators of the external sites are responsible for subject recruitment, obtaining Informed Consent, assessment of inclusion and exclusion criteria and assessment of hearing and medical history related to this umbrella Clinical Investigation Plan. Subjects may then be referred to the sponsor principal investigator of internal (Cochlear) sites, who will conduct the remaining study procedures as described in the umbrella and sub-study Clinical Investigation Plan. Section 10 describes the Informed Consent process.

The following scenarios for sub-studies are distinguished:

- The sponsor principal investigator or study staff of internal (Cochlear) sites will conduct study procedures at the facilities of internal (Cochlear) sites. The conduct of the study procedures is the responsibility of the sponsor principal investigator.
- The sponsor principal investigator or study staff of internal (Cochlear) sites will conduct study procedures at the facilities of the site of the external principal investigator. The conduct of these study procedures remains the responsibility of the sponsor principal investigator of internal (Cochlear) sites.
- The external principal investigator or study staff of external site(s) will conduct study procedures at the facilities of the site of the external principal investigator. The conduct of the study procedures is the responsibility of the external principal investigator.
- The external principal investigator or study staff of the external principal investigator will conduct study procedures at the facilities of internal (Cochlear) sites. The conduct of these study procedures remains the responsibility of the external principal investigator.

For all scenarios, the coordinating investigator of the sub-study is the coordinating investigator of the umbrella investigation. Study staff (e.g. technical expert) of the external site(s) of the umbrella study may conduct study procedures for which the sponsor principal investigator of a sub-study is responsible, only in case the study staff have the qualification and competence to conduct these study procedures. The conduct of these study procedures is the responsibility of the sponsor principal investigator.

In each sub-study, the new method/tool will be evaluated by using a set of tests. A detailed description of the tests that will be used shall be provided in the sub-study specific documentation. The scope of this study will include tests such as those given in Table 1. As a part of these tests and as mentioned in section 7.1 the subject might be asked to complete questionnaires, to perform at-home tests etc. during the take home use.

Evaluation of each method will be done by a repeated-measures design, in which each subject is acting as his/her own control. Some methods/tools will be tested in acute laboratory sessions, while others will require take-home experience to be able to fully evaluate the benefit and provide feedback by the user. In case a take-home trial will be performed, the IMD will be provided to the subject for real life listening experience. Tests may be repeated. When applicable, a cross-over study design will be used during another evaluation session after completion of the second set-up/test condition. Subjects may revert to their own sound processor programs, if in a situation where it is felt that performance is not sufficient with the new programs.

At the end of each sub-study, the investigational software and/or firmware will be taken off the sound processor, remote control or mobile device and the subject will go back to his/her own program.

The time for a clinical visit will be limited to a maximum of 4 hours. The time in between clinical visits will vary with typical spacing of between 0 (acute) to 4 weeks.

The following activities might be applied:

a) Review of MAP/Clinical History

The subject's latest available cdx file (a file containing the 'map' or fitting for that specific subject) will be imported into the Custom Sound database as sent from the recipient's local clinic.

b) Programming (if applicable)

- Different programs will be created using different programming methodologies.
- The software will be used by the clinician or professionals or by recipients themselves.
- The order of creating the programs will be randomised and balanced across subjects where possible according to the subject's study number.
- A screen recording of the computer, tablet or mobile device and / or video recording may be done for programming tasks when required and where agreed by the recipient.

c) Take home use (if applicable)

- The new programs may be loaded to a loaner sound processor in a randomised and balanced order.
- Subjects will be asked to use the new programs or software in real world environments and provide feedback.
- Subjects will be encouraged to record their daily experiences in the daily diary or other questionnaires if applicable.
- Subjects might be asked to perform at-home tests etc. during this take home use.

d) Evaluation

The tests used for evaluation will be specified at sub-study level. Table 1 shows an overview of possible tests that can be conducted. Not all tests may be relevant for every sub-study, naturally, unnecessary tests will be skipped. If applicable, a new diagnostic method is used (i.e. adaptation to one of the methods as shown in Table 1).

- Speech perception in free field can be conducted.
- Speech perception tests may also be conducted by delivering inputs directly to the sound processor through investigational software and firmware.
- The evaluation tool will be used by the professionals, by recipients or parents/legally designated representatives.
- If applicable and available, the subjects might be asked to perform at-home tests in between visits and/or at the clinical visits.
- The order of the tests will be randomised, blinded and balanced where possible.
- If applicable, the clinician may be asked to provide feedback on the ease of use of the new method and its training materials.

Table 1: Example of a post-operative test battery

Nr	Test	Description
1	Tonal Audiometry	Standard tonal audiogram.
2	Phoneme detection and discrimination tests	Evaluation of the peripheral auditory function (cochlea) by the test of phoneme detection and discrimination.
3	Speech in quiet	Standard audiological word tests in quiet.
4	Speech in noise	Word and sentence tests in noise, with noise either at a fixed level or adaptively adjusted.
5	Objective measures	e.g. Electrical measurement of the compound action potential of the auditory nerve, pupillometry, impedance measurements etc.
6	Questionnaire	Questionnaires to ask subjects feedback on certain features of the system, sound quality, ease of use, music appreciation etc.
7	Video tape	Subjects may be videotaped when agreed to and when required.
8	Psychophysics	Psychophysical experiments may be performed to test how sensitive implant users are to small differences between stimuli and to rate the quality of the different stimuli. For example, we may present 2 different sounds (varying in loudness or pitch) and ask subjects to rank their loudness or pitch.
9	Directional hearing test	Multiple speakers in surround set-up. Subject is asked to indicate where the sounds come from.
10	Diary	Subjects may be asked to keep track of e.g. battery usage, report on the different listening environments they were in, how they experienced the effect of the new program/tool etc.
11	Device metrics	State of the art cochlear implant systems have in-built data logging containing device diagnostics and statistics on the use of the device, on the sound environment etc.

12	Language development tests	Monitor the language development of young children may be done by taking standardized tests on receptive and expressive language skills, such as the Peabody Picture Vocabulary Test, Reynell Test, Schlichting Test, Preschool Language Scale (PLS) or Clinical Evaluation of Language Fundamentals (CELF).

Intra-operative stage to collect objective measurements:

Only CE approved devices will be used for this intra-operative testing in accordance with the approved indication(s) and terms of the market authorization.

The investigator may request a nurse, the surgeon or a clinician to run the test under the investigator's supervision.

Video recording may be done during the testing where required.

If the intra-operative tests take significantly more time under anaesthesia (as judged by the surgeon) the testing will be aborted.

Post-operatively, these subjects might be recruited following the procedures as described for the group 1 subjects.

Where possible the comparing measurements will be provided blinded to subject and/or tester.

Subjects can participate in several sub-studies (one at a time).

The results of the tests will be carefully monitored during the study and compared with the baseline results and with the benchmark results (where applicable) typical for each category of subjects.

A detailed description of the procedure shall be provided in the sub-study specific documentation.

7.4 Safety Evaluations and Procedures

The risks and anticipated ADEs for the investigational device, 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 for every sub-study.

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

In case of concomitant medication, this is administered as part of the safety Clinical Report Forms.

Possible interactions with concomitant medications are not anticipated in this clinical investigation. Information on baseline concomitant medication (all medications related to hearing health, balance or known ototoxic) will be collected during enrollment for each sub-study. In the event of AE's and ADE's, any medications taken in relation to these events will also be collected.

7.5 Equipment Used for Evaluation of Performance and Safety

The used equipment, the monitoring, maintenance and calibration will be described in the sub-study documentation.

7.6 Sponsor Role in Conduct of the Clinical Investigation

As mentioned in section 7.3, the sponsor principal investigator of the internal (Cochlear) sites may conduct study procedures upon referral of subjects from the external principal investigator. Section 10 describes the Informed Consent process. The procedures performed by the sponsor principal investigator will be clearly described in the sub-study documentation.

There is no mitigation for potential bias to the data integrity. Where possible, a sub-study will be blinded.

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

8.1 Anticipated Clinical Benefits

Potential direct benefits for subjects associated with participation in the clinical investigation include:

- New diagnostics, programming and/or (re)habilitation methods may result in increased hearing performance or sound quality comparing to the baseline condition and/or may be preferred by the recipient. In this case, the subject may have access to the program at the end of the study if the CE approval is obtained and after proper consultation with the recipient's hearing professional.

Potential indirect benefits include:

- New methods may result in an increased efficiency of time for clinicians and provide a more consistent outcome for their CI recipients. Also, in this case the clinician is free to retain the preferred method as soon as the necessary CE approval is obtained and when the CI recipient agrees to this new method.
- Through this clinical investigation Cochlear may bring product improvements to the market that will benefit all cochlear implant users.

8.2 Anticipated Adverse Device Effects

The subjects of this umbrella investigation are already implanted or will be implanted with a CE approved Nucleus implant device, independent of this study. No medication will be prescribed for the study.

The nature of the investigation is purely hearing therapy related, namely either fitting, diagnostics or (re)habilitation. The electrical stimulation can be somewhat different from an approved sound processor device due to changes in the software or firmware. The risks associated with this change are listed below.

The expected risks with use of CE approved sound processors are described in the Investigator's Brochures (IB) and in the Instruction For Use (IFU). Adverse device effects specific to this study (i.e. not cochlear implants in general) include the following audiological risks:

Uncomfortably loud stimulation: Since every subject has a different sensitivity to the electrical stimulation, some levels of stimulation may be provided at a level perceived as being too loud even though they are safe from a biological perspective. This hazard has the largest residual probability, but

the severity is limited to discomfort. This hazard is essentially controlled during fitting of the implant. Fitting is a key step of the investigational studies and the associated risk is not exceeding the risk during normal clinical handling of a CI. To mitigate this risk, the same level of control measures is implemented in the software as in the standard clinical fitting software. Furthermore, the fitting is conducted or overseen by an experienced clinician.

Note that during previous umbrella studies (CTC5585 'Innovation in Clinical Care for Users of a Nucleus Cochlear Implant' and CTC5595 'Innovation in Sound Coding for Users of a Nucleus Cochlear Implant') where programming was involved, one subject reported a louder stimulation than comfortable (pain) during programming. The uncomfortable stimulus was immediately stopped and the issue was resolved. A second subject reported a headache during the measurements, which resolved after some time.

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

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

Sub-optimal fitting of the device resulting in sub-optimal performance: It is possible that investigational alternatives result in a decline of hearing outcomes. It is well known that some types of changes to a map may lead to an acute minor decline in hearing outcomes. As the CI user adapts to the new sound quality, this decline is often temporary. But in the worst case a user may not adapt, and he/she may decide not to wear the sound processor anymore, resulting in an absence of hearing. In this study a CI clinician will be available to provide hearing care, and address reports of degraded performance. Subjects will also have access to their standard baseline map that they can return to at all times. Again, this risk is similar to the risk in normal clinical management.

In the case of prolonged observed systematic decrease in performance the particular test set-up/condition can be halted. Subjects can always revert to their baseline map as this is kept available to them. After the study has been finished, the patients will return to their original/preferred strategy/condition.

Intra-operative testing only: There is a risk that the intra-operative tests take longer and lengthen the time the subject is under anaesthesia. In this case the surgeon or anaesthetist can abort the testing.

In summary, the risks involved with the investigational devices are not substantially different from the risks associated with normal CI users and the normal clinical handling of a CI.

8.3 Risks Associated with Participation in the Clinical Investigation

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

- Impact performance if new programming, diagnostic and (re)habilitation methods may involve inconveniences and discomfort with increased listening practice/effort.
- Inconveniences related to attending study sessions and completing study procedures.

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

8.4 Risk Mitigation

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

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

- Detailed study procedures are provided for each sub-study to the investigator to mitigate the risks of inappropriate use of the investigational device.
- Investigators are trained to avoid over-stimulation and/or non-auditory stimulation and the recipient has the possibility to remove the coil of the sound processor from their head to stop stimulation.
- Subjects will be provided with the Instruction For Use of the applicable commercial sound processor used during the clinical investigation.
- Subjects may revert to using their own Nucleus sound processor programs, if in a situation where it is felt that performance is not sufficient with the new program(s).
- Adverse events will be collected as described in section 11.

8.5 Risk-to-Benefit Rationale

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

The potential temporary inconveniences and discomforts associated with participation in one or more sub-studies under this umbrella investigation is proportional to the potential direct short-term benefits possible increased hearing performance, or indirect benefits, as described in section 8.1.

9 STATISTICAL CONSIDERATIONS

9.1 General Considerations

Data will be analysed separately per sub-study. Analysis of the data will take place at Cochlear. Sub-study specific endpoints and other statistical considerations such as hypothesis and sample size

determination will be described in the sub-study documentation and a sub-study CIR will be written when these endpoints are reached.

9.2 Endpoints

Each sub-study addresses aspects of one or more of the innovations described in section 4.1. Sub-study specific endpoints and details such as specific measurements and time points for assessment of each measure, will be described in the sub-study documentation.

9.2.1 Primary Endpoint

Monosyllabic word in quiet scores (for standard-of-care and new/optimized device fitting methods).

9.2.2 Secondary Endpoints

There are no secondary endpoints stated in the umbrella investigation, however, will be specified in the sub-study documentation if appropriate.

9.2.3 Exploratory Endpoints

There are no exploratory endpoints stated in the umbrella investigation, however, they will be specified in the sub-study documentation if appropriate.

9.3 Hypotheses

Sub-study specific hypotheses and details such as margins for the hypothesis's tests, will be described in the sub-study documentation.

9.3.1 Primary Hypothesis

There are no primary hypotheses stated in the umbrella investigation, however, they will be specified in the sub-study documentation.

9.3.2 Secondary Hypotheses

There are no secondary hypotheses stated in the umbrella investigation, however, they will be specified in the sub-study documentation if appropriate.

9.3.3 Exploratory Hypotheses

There are no exploratory hypotheses stated in the umbrella investigation, however, they will be specified in the sub-study documentation if appropriate.

9.4 Sample Size Determination

This umbrella study explores the feasibility phase of new or improved fitting, diagnostic and (re)habilitation software, research fitting and research diagnostic tools.

Sample size requirements will be described in the sub-study documentation. A maximum of 160 subjects will be recruited to participate in sub-studies under this umbrella investigation.

9.5 Analysis Populations

A detailed description of the statistical analysis that will be used for each sub-study will be described in the sub-study documentation.

9.6 Primary Endpoint Analyses

Primary endpoint analysis will be done on the level of the sub-study. A detailed description of the statistical analysis will be specified in the sub-study documentation.

9.7 Secondary Endpoint Analyses

There are no secondary endpoints stated in the umbrella investigation, however, they will be specified together with a detailed description of the statistical analysis in the sub-study documentation if appropriate.

9.8 Exploratory Endpoint Analyses

There are no exploratory endpoints stated in the umbrella investigation, however, will be specified together with a detailed description of the statistical analysis in the sub-study documentation if appropriate.

9.9 Safety Analyses

Per sub-study adverse events will be listed by verbatim term, according to severity, seriousness and relationship to the investigational device and investigation procedures. Also, device deficiencies will be listed by verbatim term.

9.10 Interim Analyses

Not applicable, unless specified differently in sub-study documentation.

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 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.

The external principal investigator or study staff of external principal investigator shall be responsible for subject recruitment and obtaining Informed Consent for the umbrella investigation AI5763. Each sub-study will have its own sub-study specific ICF in which the detailed procedure of the sub-study is described. All other aspects such as insurance and privacy verbatim of the ICF of umbrella study AI5763 still apply.

The principal investigator or study staff responsible for the conduct of the sub-study will obtain Informed Consent for each sub-study. The sponsor principal investigator of CTC/Cochlear, Melbourne will always receive a copy of the signed Informed Consent Form of AI5763 and the sub-study.

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 or CIP.

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

11.1.6 Adverse Events of Special Interest

There are no Adverse Events of Special Interest.

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 of the sub-study and the investigator should enquire about AEs at investigation visits.

All AEs will generally be recorded on sub-study basis from the time of treatment assignment and continue for each subject until completion of their End of Study visit. Where the involves acute treatment only, AE will be recorded only from the time of treatment assignment and continue for each subject until 4 hours after their study visit. Ongoing SAEs and SADEs will be followed for 30 days, or until resolution or stabilisation of the event, whichever comes first. Any variations to these requirements will be documented in each sub-study documentation (for example, variations to account for in-booth only or take-home use).

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 assess the 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/ Instruction For Use (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 IB are anticipated ADEs.

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

11.3 Recording and Handling of Device Deficiencies

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

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

1) suitable action had not been taken,

2) intervention had not been made, or,

3) circumstances had been less fortunate

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

11.4 Reporting Responsibilities

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

11.4.1 Investigator Reporting of Serious Adverse Events

All AEs meeting the criteria for an SAE, or DD that could have led to a SADE, must be reported to the Sponsor without delay.

Reporting is achieved through completion of the events details in the Adverse Event page of the electronic Case Report Forms (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 Ethics Committee (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 a SADE.

CTC: The sponsor is responsible for reporting to the FAMHP (Federal Agency for Medicines and Health Products): ct.rd@famhp.be, by using the MDCG 2020-10/2 form: (a) any serious adverse event that has a causal relationship with the investigational device, the comparator or the investigation procedure or where such causal relationship is reasonably possible; (b) any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate; and (c) any new findings in relation to any event referred to in points (a) and (b).

Reporting must be: a) for all reportable events which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding to it: immediately, but not later than 2 calendar days after awareness by sponsor of a new reportable event or of new information in relation with an already reported event; or b) any other reportable events or a new finding/update to it: immediately, but not later than 7 calendar days following the date of awareness by the sponsor of the new reportable event or of new information in relation with an already reported event. In case an initial notification of an SAE/SADE would be incomplete, on receipt of additional information the Sponsor must submit a clearly referenced and numbered follow-up report of the event.

Cochlear Melbourne: The sponsor is responsible for reporting serious adverse events (SAE) that occur in Royal Victorian Eye and Ear Hospital participants to the Human Research Ethics Committee as soon as possible and within 72 hours of occurrence. All internal SAEs (occurring in Eye and Ear participants) must be reported to the Eye and Ear HREC as soon as possible and within 72 hours of occurrence. External SAEs (occurring in participants at other sites) must be reported in a prompt manner if the information would reasonably be expected to adversely affect the continued ethical acceptability of the trial. This includes cases where the information would lead the HREC to require a change in the trial protocol or information statement, including changed monitoring (using the Single SAE form). The Sponsor is required to report to the Therapeutic Goods Administration any fatal or life-threatening Australian USADEs, and all other Australian USADEs within 7 and 15 days respectively.

The Safety Monitor for AE/DD assessment and any AE/DD related queries can be contacted via CLTD-SafetyMonitor@cochlear.com.

11.5 Independent Data Monitoring Committee

Given the low residual risk associated with this study (such as no changes to the implant, no significant changes to the stimulation pattern, only minor changes to the sound processor firmware, absence of surgical risk, audiological risk comparable to clinical follow-up), an IDMC will not be established for this study.

12 DEVICE ACCOUNTABILITY

Supply of investigational medical devices will be recorded using tracking forms such as the Sponsor Device Tracking Form (1295388) and Software Tracking Form (1302326). 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 Individual Subject

Device Accountability Log Form (1295295). At the end of the clinical investigation, all investigational medical devices shall be returned to the Sponsor. In cases where a commercially released product is required to facilitate the functionality of the investigational device, the commercial product shall be registered following the standard product registration process.

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

Name of contact person of the Sponsor:	[redacted]
Country and time zone:	Belgium (GMT+1)
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, within ample time 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

On umbrella study level information about eligibility, demographics, medical, hearing and device history, protocol deviations and completion of study will be obtained. On sub-study level also adverse event, device deficiency and sub-study specific information will be captured.

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, questionnaires or printed directly from testing software. Data such as clinical performance data, questionnaires etc. can be entered directly into the eCRF which shall be considered source data for these items. If electronic medical records do not permit read only access for monitoring purposes, a certified printout must be provided.

The system used for data collection will be specified at the sub-study level, including the use of electronic data capture (EDC) on eCRFs.

In addition, de-identified electronically generated data will be collected from clinical fitting software, objectives measures software, imaging (such as CT), videography, diagnostic tools etc. The unamended data file shall be regarded as the source.

In case the full eCRF option is not utilized, data collection for demographics, device exposure, medical history, adverse events, device deficiencies, concomitant medications, protocol deviations and completion will be performed using electronic data capture (EDC) on electronic Case Report Forms (Safety eCRF), to support safety analysis and reporting. All other data will be collected from clinical fitting software, objectives measures software, imaging, videography, clinical performance data etc. or captured into paper Case Report Forms and entered in a suitable database or directly into the study report after review by the study monitor. In case specific procedures are used for data management such as data collection and review, this will be specified in the sub-study documentation. Site personnel will be trained on the completion of the CRFs. Unamended data files shall be regarded as the source.

Site personnel will be trained on the completion of the eCRF prior to obtaining access to the system and will have their own Login/Password. Access to clinical study information will be based on an individual's role and responsibilities.

The eCRF will have 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 (e.g. 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

In case of a blind sub-study, the criteria for access to and breaking the blinding/masking code in the case of suspension or premature termination of the clinical investigation will be described in the sub-study documentation.

CTC: Upon end of a clinical investigation, the sponsor shall notify the regulatory authority within 15 days. In the case the clinical investigation is temporarily halted or terminated early, notification of this shall be made to the regulatory authority within 15 days. Justification for the halt or termination shall be included. If either situation is on safety grounds, then the reporting timeframe is 24 hours.

Cochlear Melbourne: If a trial is prematurely terminated or suspended, the sponsor should promptly inform the investigator(s), institution(s), the ethics committee, and the TGA. The sponsor should provide the reason(s) for the termination or suspension.

18 AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

No changes in the CIP or investigation procedures shall be made without mutual agreement of the Principal Investigators 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 retrospectively registered at a public clinical trial registry ClinicalTrials.gov. Due to the local Ethics Committee requirement, the results from sub-studies with participation from Melbourne sites will be reported in the public clinical trial registry.

A joint peer-reviewed publication authored by the clinical investigator(s) and Sponsor may be prepared. In addition, the results of the clinical investigation may also be disseminated as conference presentations (for example abstract and poster session). Manuscript authorship and responsibilities will be discussed and agreed upon prior to investigation start and in accordance with guidelines and recommendations provided by the International Committee of Medical Journal Editors (ICMJE) to enable communication in a timely manner. All contributors who do not meet the criteria for authorship will be listed in an acknowledgments section of the publication.

Further details are described in the Clinical Investigation Research Agreement (CIRA) of the 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 initiation, monitoring and close out.

The monitoring plan is described at umbrella level. In case monitoring differs from this monitoring plan for a specific sub-study (e.g. more monitoring is required), an additional sub-study monitoring plan will be created.

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 or its designee 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

1) Botros, A., Banna, R., & Maruthurkkara, S. (2013). The next generation of Nucleus(®) fitting: A multiplatform approach towards universal cochlear implant management. International Journal of Audiology, 52(7), 485–94.

2) Clinical investigation of medical devices for human subjects — Good clinical practice. International Organization for Standardization, ISO 14155.

3) Medical devices — Application of risk management to medical devices. International Organization for Standardization, ISO 14971.

4) 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/.

5) Safety reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745. Medical Device Coordination Group (MDCG), MDCG 2020-10/1 and 2020-10/2.

25 CHANGE HISTORY

Version	Change	Rationale
1.0	Introduction CIP	NA
2.0	Section 17: "Upon end of a clinical investigation, the sponsor shall notify the regulatory authority within 15 days. In the case the clinical investigation is temporarily halted or terminated early, notification of this shall be made to the regulatory authority within 15 days. Justification for the halt or termination shall be included. If either situation is on safety grounds, then the reporting timeframe is 24 hours."	Specified the process of reporting end of a clinical investigation to the regulatory authority.
3.0	Section 11.4.2: "The sponsor is responsible for reporting serious adverse events (SAE) to Famhp (Federal Agency for Medicines and Health Products): ct.rd@famhp.be, by using the European form. Reporting must be a) immediately for any SAE or device deficiency (DD) that might have led to a SAE resulting in death or threat to life, or is associated with imminent risk of death, or for any serious injury or disease warranting rapid curative therapy or any new information relating thereto, and b) immediately and in any case no later than 7 days for other SAE/SADEs. In case an initial notification of an SAE/SADE would be incomplete, on receipt of additional information the Sponsor must submit a clearly referenced and numbered follow-up report of the event."	Specified the process of reporting adverse events to the regulatory authority.
4.0	Updated sponsor details on pages 1 and 2; added CRO details in page 2; updated number of subjects, number of sits and inclusion criteria in synopsis; updated section 5.1 (deleted information on risk management and device control, has been mentioned in	Cochlear Melbourne (internal site) and HEARnet, Melbourne (external site) have been added as additional sites under the current umbrella study. Details regarding the updated subject numbers, sites and associated reporting requirements to competent authority and ethics have been added. Inclusion criteria has been modified to

	risk mitigation section 8.4); updated section 7.2.1 inclusion criteria, updated section 7.2.3 for subject numbers; section 7.2.4 for additional details regarding children to be tested in Belgium only, updated language in section 7.2.5; updated section 7.3 for additional sites details; updated section 7.4.1 concomitant medications; updated section 8.2 to add details of risks reported in earlier relevant clinical studies; section 11.4.2 Sponsor Notification of Events (added details about Melbourne); section 14 data management (some of the information has been transferred to section 7.2.5); section17 Suspension or Premature Termination (added Melbourne details); section 20 updated Trademarks as of 2020	reflect that only adults will be recruited in Australia, however in Belgium both adults and children can be recruited. Additional changes made include changes in terminology as per the new cochlear template and typos. Section on concomitant medications has been updated to specify the medications information that will be collected as part of this study.
5.0	Section 11.4.2 update of reportable safety events and timelines.	Change in safety reporting to the regulatory authorities as per EU Medical Device Regulation 2017/745 (MDR), Article 80 (2)
6.0	Deletion of not registering on a public clinical trial registry. Addition of clarification to the number of subjects in this feasibility trial. Addition of primary endpoint, separation of primary and secondary objectives. Change of time in between clinical visits from 1-4 weeks to 0 (acute)-4 weeks. Addition of AE recording and handling for acute visits. Addition of registration to public clinical trial registry details. Updated trademarks and copyrights	Local Ethics Committee requirement to register on a public clinical trial registry. Clarification to the number of subjects in this feasibility trial. Majority of research to involve fitting methodology evaluation. Consistent outcome measure will be monosyllabic words in quiet in all sub-studies targeting fitting methodologies. To correct the time in between clinical visit as stated in the CIP. Additional clarification on AE recording and handling for acute visits. Additional clarification of registration to public clinical trial registry and what will be reported. Update to the current trademarks and copyrights

Signature Page for [redacted] v6.0

Reason for signing: Approved	[redacted] Date of signature: 19-Apr-2022 08:44:13 GMT+0000

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