STUDY PROTOCOL – COVER PAGE

Title: Clinical Investigation of the safety and performance of HiRes™ Ultra CI HiFocus™ MS Electrode (CI-1600-04) and HiRes™ Ultra 3D CI HiFocus™ MS Electrode (CI-1601-04) (Ultra X) in adults with severe-to-profound hearing loss

Sponsor: Advanced Bionics AG

Project ID: ABIntl-19-44

ClinicalTrials.gov ID: NCT04610112

Date of the document: 12 January 2022

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Clinical Investigation of the safety and performance of HiRes™ Ultra CI HiFocus™ MS Electrode (CI-1600-04) and HiRes™ Ultra 3D CI HiFocus™ MS Electrode (CI-1601-04) (Ultra X implants) in adults with severe-to-profound hearing loss

Project ID: ABIntl-19-44

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Principal Investigator II	
Principal Investigator III	
Principal Investigator IV	

Name(s) and address(es) of other institutions involved in the clinical investigation

CIP approval page

Study title: Clinical Investigation of the safety and performance of HiRes™ Ultra CI HiFocus™ MS Electrode (CI-1600-04) and HiRes™ Ultra 3D CI HiFocus™ MS Electrode (CI-1601-04) (Ultra X) in adults with severe-to-profound hearing loss

Study compliance: ISO 14155:2011, 90/385/EEC
ICH-GCP and Declaration of Helsinki

AB Study Number/ CIP Number: ABIntl-19-44
09/07/2020

Summary of the revision history in the case of amendments no ammendments

Protocol Commitment – Signatures

We have read and understood this protocol and agree on its content. We agree to conduct the study in accordance with the compliance and commitments as stated in this protocol. In addition, the signatories of this protocol (below) and delegates will assume responsibility for protocol compliance for persons to whom they delegate study related tasks. This document is the property of AB AG. It is at confidential disposal to the study participants. It may not be used, divulged, published or otherwise disclosed without the consent of the Coordinating Investigator and the Advanced Bionics Senior Manager of Clinical Research. **(Please Use blue ink)**

[redacted]

Name of **Principal Investigator I**:_____

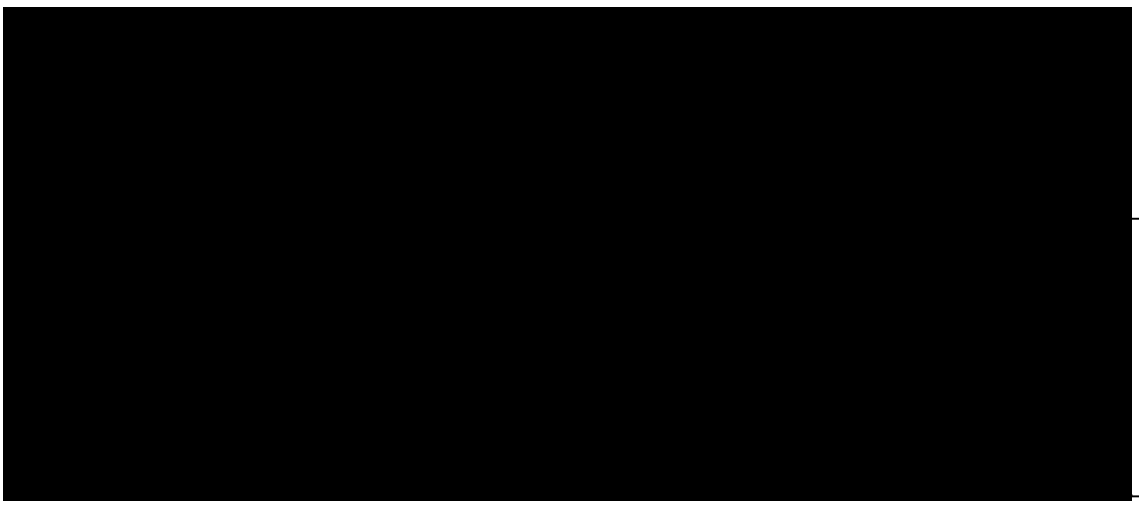
Date: _____ Signature: _____

Name of **Principal Investigator II**:_____

Date: _____ Signature: _____

Name of **Principal Investigator III**:_____

Date: _____ Signature: _____



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Name of **Principal Investigator III**:_____

Date: Signature:

Centre **IV**:_____

CIP approval page

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Name of **Principal Investigator III**:_____

Date: Signature:

Centre **IV**:_____

Name of **Principal Investigator IV**:_____

Date: Signature:

[redacted]

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List of Abbreviations

AB AG	Advanced Bionics, AG
ADE	Adverse Device Effect
AE	Adverse Event
CIP	Clinical Investigation Plan
CPM	Clinical Project Manager
CRF	Case Report Forms
eCRF	electronic CRF
ePTFE	fluorocarbon polymer
dB	Decibel
DMC	Data Monitoring Committee
E-Field [V/m]	Electric field [volt per meter]
FU	Follow Up
HA	Hearing Aid
HFMS	HiFocus Mid Scala electrode array
Hz	Hertz
ICF	Informed Consent Form
ICS	implantable cochlear stimulator
kV/m	kilovolt per meter
M-field [A/m]	Magnetic Field [Ampère per meter]
MHz	Megahertz
OlSa	Oldenburger Satztest (Oldeburger sentence test)
PMCF	Post Marketing Clinical Follow up
RF	Radio Frequency
RW	Round Window
QMS	Quality Management System
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SRT	Speech Reception Threshold
T	Tesla
TENS	Transcutaneous Electrical Nerve Stimulation
UADE	Unanticipated Adverse Device Effect

1.0 Clinical Investigation Synopsis

Study Title	Clinical Investigation of the safety and performance of HiRes™ Ultra Cl HiFocus™ MS Electrode (Cl-1600-04) and HiRes™ Ultra 3D Cl HiFocus™ MS Electrode (Cl-1601-04) (Ultra X) in adults with severe-to-profound hearing loss
Sponsor	Advanced Bionics AG
Device	HiRes™ Ultra 3D Cl HiFocus™ Mid-Scala Electrode (CI-1601-04) HiRes™ Ultra Cl HiFocus™ Mid-Scala Electrode (CI-1600-04)
Study Design	Prospective within-subjects repeated-measures design where each subject serves as his/her own control
Regulatory Objective	Post Market Clinical Follow
Study Population	30 adult subjects with valid and useable data
Inclusion Criteria	• No previous experience with any auditory implant • 18 years of age or older • Postlingual onset of severe hearing loss (≥ 4 years of age) • Limited benefit from appropriately fitted hearing aids, defined as scoring 60% or less in Freiburger Monosyllabic word test • German language proficiency • Willingness to participate in all scheduled procedures outlined in the protocol
Exclusion Criteria	• Cochlear malformation or obstruction that would preclude full insertion of electrode array. • Presence of additional disabilities that would prevent or interfere with participation in the required study procedures • Medical or psychological conditions that contraindicate surgery or impact the ability to manage an implanted device or the study related procedures • Evidence of central auditory lesion or compromised auditory nerve • Pregnancy at time of surgery.
Primary Efficacy Objective	The primary efficacy objective is to demonstrate that mean monosyllabic word recognition score with the Ultra X used in combination with a sound processor programmed with the latest fitting software is at least 20% better than the mean monosyllabic word score at baseline with conventional amplification in the same ear.
Secondary Efficacy Objective	The secondary efficacy objective is to demonstrate that mean sentence score in noise with the Ultra X are equal or better than sentence scores in noise at baseline with conventional amplification in the same ear.
Primary Safety Objective	The primary safety objective is to document any adverse events related to Ultra X that require device replacement.
Primary Efficacy Endpoint	The primary efficacy endpoint is the Freiburger monosyllabic word recognition score in the implanted ear six months after device activation compared to the baseline score with a hearing aid in the same ear.
Secondary Efficacy Endpoint	50% speech reception threshold in the Oldenburger Sentence Test (OlSa) in noise in the implanted ear six months after device activation compared to

	baseline performance with conventional amplification in the same ear.
Primary Safety Endpoint	A maximum of one device failure that require device replacement during the first six months following device activation (activation approximately one to eight weeks after surgery).
PMCF objective (if required)	Primary and secondary efficacy objectives and safety objectives are the PMCF objective.
Additional Interest	• Device fitting data, especially M-level and impedances • Feedback of the audiologist using the latest fitting software to program the latest processor • Feedback from the surgeon on handling of the device and tools during implantation • Using habits of participants as summarized in the logging of the processor and assessed in a patient questionnaire • Monitoring of potential adverse events
Additional Evaluation	• Descriptive statistics for questionnaire rating of the surgeons, audiologists and patients; categorizing and trending of comments • Descriptive statistics and further statistical analysis of fitting and logged data, e. g. on duration of use and classified environment
Study Schedule	• Consent: Subject will sign ICF prior to conduct of any study procedures. • Baseline: Assessment of auditory perception abilities aided with conventional amplification (standard of care, aided and unaided hearing thresholds, word score in quiet, sentences in noise with OlSa), patient questionnaire • Surgery: Following standard of care Surgical questionnaire after each implantation • Device activation (approximately one to eight weeks after surgery) Auditory perception abilities aided with CI (standard of care, hearing thresholds), questionnaire for the audiologist • 3 months post device activation: Auditory perception abilities aided with CI (standard of care, hearing thresholds, word score in quiet, sentences in noise with OlSa), patient questionnaire, questionnaire for the audiologist • 6 month post device activation: Auditory perception abilities aided with CI (standard of care, hearing thresholds, word score in quiet, sentences in noise with OlSa), patient questionnaire, questionnaire for the audiologist
Follow-up Schedule	6 months after initial device activation subjects will continue to receive their CI after-care in clinical routine
Study Monitoring	According to ISO 14155
Statistical Analyses	Three and six months speech perception scores will be compared to baseline scores using applicable parametric or nonparametric statistical analyses. Questionnaire data will be summarized using frequency and relative frequency.

1.1 Synopsis (deutsch)

Studientitel	Klinische Untersuchung der Sicherheit und der Leistungsfähigkeit von HiRes™ Ultra CI (CI-1600-04) und HiRes™ Ultra 3D CI (CI-1601-04) mit der HiFocus™ MS Elektrode (Ultra X Implantate) in hochgradig ertaubten Erwachsenen
Sponsor	Advanced Bionics AG
Produkt	HiRes™ Ultra 3D CI HiFocus™ Mid-Scala Elektrode (CI-1601-04) HiRes™ Ultra CI HiFocus™ Mid-Scala Elektrode (CI-1600-04)
Studiendesign	Prospektive Studie mit wiederholten Messungen beim gleichen Patienten, die miteinander verglichen werden; die Ausgangsdaten bei Studienaufnahme dienen jeweils als Kontrolle
Regulatorische Zielsetzung	Post Market Clinical Follow
Studien-Population	30 Erwachsene mit gültigen und verwertbaren Datensätzen
Einschluss-Kriterien	• Bisher keine Erfahrung mit einem auditorischen Implantat-System • 18 Jahre oder älter • Postlingualer Beginn einer starken Hörstörung (≥ 4 Jahre) • Nur begrenzter Nutzen von Hörgeräten, definiert als ein Sprachverständnis von 60% oder weniger im Freiburger Einsilber-Test • Deutschkenntnisse • Bereitschaft, an allen im Studienprotokoll beschriebenen Maßnahmen teilzunehmen
Ausschluss-Kriterien	• Cochleäre Missbildung oder Obstruktion, die eine vollständige Insertion des Elektrodenträgers verhindern würde • Zusätzliche Einschränkungen, die eine Teilnahme an den Studien-Maßnahmen beeinträchtigen würden • Medizinische oder psychologische Voraussetzungen, bei denen eine Operation kontraindiziert ist, die die Fähigkeit der Implantat-Handhabung oder die Teilnahme an den Studienprozeduren einschränken würden • Hinweise auf zentral-auditorische Läsionen oder Beeinträchtigungen des Hörnervs • Schwangerschaft zum Zeitpunkt der Operation.
Primäres Wirksamkeitsziel	Das primäre Wirksamkeitsziel ist zu zeigen, dass das mittlere Verstehen im Freiburger Einsilbertest mit dem Ultra X in Kombination mit dem aktuellen Prozessor und Anpasssoftware mindestens 20% besser ist als das mittlere Einsilber-Verstehen zu Beginn der Studie mit konventioneller Versorgung auf der gleichen Seite.
Sekundäres Wirksamkeitsziel	Das sekundäre Wirksamkeitsziel ist zu zeigen, dass das mittlere Sprachverstehen in Geräusch mit dem Ultra X gleich oder besser ist wie das mittlere Sprachverstehen zu Beginn der Studie mit konventioneller Versorgung auf der gleichen Seite.
Primäres Sicherheitsziel	Das primäre Sicherheitsziel ist, alle Vorkommnisse mit dem Ultra X zu dokumentieren, die eine Re-implantation erforderlich machen.
Primärer	Verstehen im Freiburger Einsilber-Test auf der implantieren Seite sechs

Wirksamkeits-Endpunkt	Monate nach der Erstanpassung verglichen mit dem Einsilber-Verstehen zu Studienbeginn mit konventioneller Hörversorgung auf der gleichen Seite
Sekundärer Wirksamkeits-Endpunkt	50%-Verständlichkeitsschwelle im Oldenburger Satztest in Geräusch auf der implantierten Seite verglichen mit der Schwelle zu Beginn der Studie mit konventioneller Hörversorgung auf der gleichen Seite
Primärer Sicherheitsendpunkt	Maximal ein Implantat-Ausfall in den ersten 6 Monaten nach Erstanpassung, der eine Re-Implantation erforderlich macht.
PMCF Zielsetzung	Primäres und sekundäres Wirksamkeitsziel sowie das Sicherheitsziel sind PMCF-Zielsetzung.
Zusätzliche Interessen	• Anpassdaten, insbesondere M-Level und Impedanzen • Rückmeldung der Audiologen zur aktuellen Anpass-Software • Rückmeldung der Operateure zur Handhabung der Implantates und der zugehörigen chirurgischen Instrumente während der Operation • Gewohnheiten der Studienteilnehmer, erfaßt über die Aufzeichnung der Prozessors sowie Patienten-Fragebogen • Verfolgen möglicher Vorkommnisse
Zusätzliche Auswertungen	• Beschreibende Statistik der Fragebogen-Einschätzungen der Operateure, Audiologen und Patienten; Kategorisierung und Trendanalyse von Kommentaren • Beschreibende und weitere Statistik der Anpassdaten und Prozessor-Aufzeichnungen, zum Beispiel zur Tragedauer oder der klassifizierten Umgebung
Ablauf der Studie	• Einwilligung: Jeder Patient unterschreibt vor Beginn der Studienmaßnahmen eine Studieneinwilligung • Ausgangsbasis: Feststellung der Hörfähigkeit mit konventioneller Versorgung (entspricht dem Behandlungsstandard, Hörschwelle, Aufblähkurve, Einsilber in Ruhe, Oldenburger Satztest in Geräusch), Patientenfragebogen • Operation: Erfolgt nach Behandlungsstandard Operateur-Fragebogen nach jeder Implantation • Erstanpassung (ungefähr eine bis acht Wochen nach Implantation) Feststellung der Hörfähigkeit mit CI (entspricht dem Behandlungsstandard, Hörschwelle), Audiologen-Fragebogen • 3 Monate nach Erstanpassung Feststellung der Hörfähigkeit mit CI (entspricht dem Behandlungsstandard, Aufblähkurve, Einsilber in Ruhe, Oldenburger Satztest in Geräusch), Patientenfragebogen, Audiologen-Fragebogen • 6 Monate nach Erstanpassung Feststellung der Hörfähigkeit mit CI (entspricht dem

	Behandlungsstandard, Aufblähkurve, Einsilber in Ruhe, Oldenburger Satztest in Geräusch), Patientenfragebogen, Audiologen-Fragebogen
Ablauf der Nachsorge	Sechs Monate nach der Erstanpassung erhalten die Studienteilnehmer die CI-Nachsorge in der klinischen Routine
Studien Monitoring	Entsprechend ISO 14155
Statistische Auswertung	Entsprechende parametrische und nicht-parametrische statistische Tests werden herangezogen, das Verstehen drei und sechs Monate nach der Erstanpassung mit den Ausgangsdaten zu vergleichen. Die Fragebögen werden nach Häufigkeit und relativer Häufigkeit ausgewertet.

2.0 Identification and description of the investigational device

- **Investigational/study Device Description**

The HiResolution Bionic Ear System is a CE approved cochlear implant designed to provide useful hearing to individuals with severe-to-profound hearing loss via electrical stimulation of the auditory nerve. The HiResolution Bionic Ear System is intended to restore a level of auditory sensation.
The HiResolution Bionic Ear System consists of internal and external components.

The internal components are either the HiRes™ Ultra Cl HiFocus™ MS Electrode or the HiRes™ Ultra 3D Cl HiFocus™ MS Electrode that are implanted surgically under the skin behind the ear. Throughout this protocol the term “Ultra X” will be used to refer to either of the implants. The electrode array has 16 contacts which are connected to the implant through the electrode lead. The receiver stimulator encapsulates the electronics into a titanium casing, the antenna coil allows for forward and backward telemetry between the implant and the external parts. The antenna coil also includes a magnet in order to retain the external headpiece. This magnet is the only significant difference between the Ultra and Ultra 3D implant. The HiRes™ Ultra Cl HiFocus™ MS electrode uses a conventional static magnet, while the magnet of the HiRes™ Ultra 3D Cl HiFocus™ MS electrode contains individually movable single magnets in a sealed housing. The movability of the individual magnets allows adjustments of the magnet in an external magnetic field, e. g. in an MRI machine.

The external components include a sound processor (body-worn or ear-level), a headpiece, and a cable. The system converts sound into electrical energy that activates the auditory nerve. The auditory nerve then sends information to the brain, where it is interpreted as sound.

Manufacturer **Advanced Bionics LLC**
25815 Westinghouse Place
Valencia, CA 91355

- **Investigational Device Model**

Product Description						
Model Number	**Product Name**	**Brief Product description**	**Sterile?**	**Single use?**	**Contact / Duration**	**Photo/Drawing**
CI-1601-04	HiRes™ Ultra 3D CI HiFocus™ MS Electrode	Implantable part of the HiResolution Bionic Ear System. Includes the HiRes™ Ultra 3D receiver and the HFMS electrode array.	Yes	Yes	Permanent contact	
CI-1600-04	HiRes^{TM} Ultra CI HiFocus^{TM} MS electrode	Implantable part of the HiResolution Bionic Ear System. Includes the HiRes™ Ultra 3 receiver and the MS electrode array.	Yes	Yes	Permanent contact	

Table 1

- **Description of traceability**

As all the products that are used in this study are commercially available on the CE market no study specific accountability will be performed. Data on which subject was implanted with which implant will be tracked according to standard clinical care. Devices are not labeled differently than those that will be used for subjects who do not participate in the study.

- **Intended purpose of the investigational device**

The HiResolution Bionic Ear System is a CE approved cochlear implant designed to provide useful hearing to individuals with severe-to-profound hearing loss via electrical stimulation of the auditory nerve. The HiResolution Bionic Ear System is intended to restore a level of auditory sensation.

- **Description of the intended population and indication**

The HiResolution Bionic Ear System is intended to restore a level of auditory sensation to individuals with severe-to-profound sensorineural hearing loss via electrical stimulation of the auditory nerve.

- **Description of the investigational device including any materials that will be in contact with tissues or body fluids**

The internal component or implantable cochlear stimulator (ICS) includes a receiver and an electrode which are implanted surgically under the skin behind the ear.
The implant electronics are contained within a hermetically sealed titanium case with a removable magnet and telemetry (RF antenna) coil attached and encased in silicone. The antenna coil assembly receives power and data over an inductively coupled link from the external sound processor system. The electrode consists of a fantail, electrode lead, and

electrode array. The electrode array (distal) is connected to the implant through the electrode lead. The lead, which extends from the fantail to the electrode array, refers to the silicone carrier in which the electrode wires are enclosed. The fantail is directly connected to the electronics in the implant. The antenna coil assembly and the electrode lead assembly connect to the electronics inside the hermetic electronics housing.
The HiFocus Mid Scala (HFMS or HiFocus MS) electrode consists of 16 platinum contacts each connected individually to sixteen insulated platinum/iridium contact wires insulated with a fluorocarbon polymer (ePTFE) in a silicone carrier. The ePTFE (higher stretch resistance) produces a more abrasion-resistant wire. The ePTFE insulation material was tested to ensure biocompatibility for chronic human implantation. The contact wire diameter allows conductivity to small amounts of stimulation pulse energy and delivers stimulation energy. The HFMS electrode is designed with materials and construction techniques to reduce the occurrence of electrode shorts and opens during manufacturing and to improve manufacturing yields.
It is also designed to give surgeons flexibility to choose among contemporary standard insertion techniques and surgical approaches (tool or off-stylet). The design of the HFMS electrode lends itself to either a small cochleostomy or round window (RW) surgical approach, which is determined by the surgeon, based upon the anatomy of the individual implant recipient and/or surgeon preference.
It also has two blue markers that are designed to facilitate visualization and consistency of insertion. The distal marker indicates the depth to which the surgeon should insert the electrode before beginning to advance the electrode off the stylet. The proximal marker indicates that full insertion has been reached. A radiopaque marker is situated under the proximal blue marker. The surgeon has the flexibility to employ either a tool or free-hand insertion.

- **Summary of the necessary training**

All required surgical and audiological training will be the same as what is required for standard clinical care.
A Surgeon's Manual and a video describing the surgical procedure and insertion of the electrode are provided to all physicians prior to implantation. Physicians must be well versed in mastoid surgery and the facial recess approach to the round window. Advanced Bionics conducts periodic training courses on the recommended surgical procedure to implant the Ultra X. Failure to obtain the appropriate training will result in a higher incidence of surgical and medical complications. Surgeons should work with an audiology professional who has been trained fully on the proper fitting and adjustment of the system.
Device and Fitting Manuals are provided to all clinical centers with the Clinician's Programming System. Audiologists must be highly skilled in administering test procedures used to determine cochlear implant candidacy according to the inclusion criteria of this PMCF. They should be knowledgeable about state-of-the-art hearing aid technology, fitting procedures as well as experience in Good Clinical Practice according to ISO 14155. In addition, at least one audiologist from a clinical center should be fully trained and qualified in the fitting of the Advanced Bionics cochlear implant. Advanced Bionics conducts periodic training courses for audiologists and strongly recommends that audiologists attend a training course. Failure to obtain the appropriate training will result in less-than-optimal patient performance.
Instructions for use for external components of the HiResolution Bionics Ear System are provided to the recipient upon delivery of the components. Patient counseling materials are

made available to all implant centers upon request. These materials provide detailed information about the system, indications for use, benefits, risks, and what is involved in patient selection, surgery, and follow-up procedures.
Further, the center will receive a training on the objective of this study, data to be obtained, any study specific procedures and the electronic data capturing system.

- **Description of the specific medical or surgical procedures**

For the implantation of the Ultra X the patient has to undergo a surgical intervention where the surgeon deploys the implant by an insertion through a skin incision (e.g. conventional incision approach; minimal incision approach) located behind the ear. The length of the incision, as well as the location of the incision itself, are decisions each implanting surgeon must consider. The titanium housing of the implant then rests in a small depression (recessed well) located in the osseous structure called the mastoid bone. A small hole in the cochlea is created at or adjacent to the round window (e.g. conventional cochleostomy, round window or a modified (extended) round window approach) and the surgeon threads the electrode array of the internal device through this hole into the cochlea. The incision behind the ear is closed so that the internal device remains beneath the skin.
Additional surgical intervention might be required if a patient must have the internal implant magnet removed to undergo an MRI scan, then the magnet replaced following MRI. For both the surgical interventions mentioned above, Advanced Bionics provides a set of surgical tools to assist the surgeon. There are two types of tools: single use sterile tools and reusable tools. The tools are optional and common OR tools can be used instead. A detailed description of the implantation methods and surgical tools is provided in the Surgeon Manuals, 029-M647-02 and 029-M725-02 for Ultra and Ultra 3D respectively. The technique used for the removal and replacement of the magnet of the Ultra 3D implant is described in the Ultra 3D Replacement Magnet and Temporary Non-Magnetic Plug Guide, 029-M785-49

3.0 Justification for the design of the clinical investigation

- **Justification for the design of the clinical investigation**

This is a prospective study designed to evaluate the safety and performance of the Ultra X under normal conditions of use as it is approved for this device. This study is set up to document any adverse events and comparing pre- to post-implant benefit to subjects. Any adverse events associated with the device will be documented via Advanced Bionics complaint handling system for the lifetime of the device. A within-subjects repeated-measures design will be employed. Speech perception will be evaluated preoperatively with conventional amplification to determine candidacy and to establish baseline performance. Efficacy parameters are speech perception data which will be collected according to clinical routine with a 6 month follow up period. Subjects will be implanted unilaterally with the Ultra X according to standard clinical care.

The primary efficacy objective is to demonstrate that mean monosyllabic word recognition score with the Ultra X used in combination with a sound processor programmed with the latest fitting software six months after activation is at least 20% better than the mean word score at baseline with conventional amplification in the same ear.
The primary efficacy endpoint is reached six months after device activation. This interval was judged to be sufficient to confirm post-implant benefit with the CI, as the majority of the

speech-perception benefit experienced by cochlear implant recipients occurs during the first few months after device activation (Koch et al., 2004; Parkinson et al., 2002; Zwolan et al., 2001, Lenarz et al. 2012). Inclusion criteria as well as the primary endpoint were derived from the "White Book for Cochlear Implantation" of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (Weißbuch Cochlea-Implantat(CI)-Versorgung, DGHNO, 2018). The White Book requires that a clinic implanting CIs shall in average achieve an improvement in monosyllabic word recognition of 20% at the end of the consecutive therapy, which is typically one year after implantation. As this study focusses on subjects without further handicap we assume to reach the 20% improvement already 6 months after first fitting. To assess further outcome parameters speech perception tests in noise (OlSa sentence test) will be conducted and subjective feedback will be collected via a questionnaire.

The primary safety objective is to document any adverse events related to Ultra X, with focus on those adverse events that require device replacement.
Primary Safety Endpoint is the maximum of one device failures that require device replacement during the first six months following device activation. Most medical/surgical complications, which are rare and have not changed significantly since the beginning of cochlear implantation, occur during surgery or shortly thereafter (Arnoldner et al., 2005; Cohen and Hoffman, 1991; Dutt et al., 2005; Green et al., 2004; Roland, 1989, Venail et al., 2008). Historical device tracking data from Advanced Bionics demonstrate that failures attributable to the implant are extremely rare. Six months after device activation is a sufficient time to document device failures that require device replacement. Thus, the success of this clinical study is contingent upon observing not more than one implant-related failure.
The inclusion criteria for the study reflects the majority of the clinical population. Subjects, which fall into the indication criteria from the IFU but from whom we do not expect reliable data or data which we can pool with other subjects will not be included. For example subjects who cannot perform a speech perception test due to additional handicaps or language proficiency will be excluded from the study, but may still fall into the indication criteria of the implant. These subjects will not deliver reliable data to support the first and second objective of this study. For market surveillance purposes these parts of the population will not be covered by this study but by other activities, like vigilance reports and surveys.

- **Evaluation of the results of the relevant pre-clinical testing**

The cochlear implant itself was qualified for long-term use in/on the human body through extensive preclinical testing using industry standards and specialized testing targeted just for cochlear implants. This testing takes into account anticipated use case stresses which could affect the stability and reliability of the device, such as: impact, flexure and tensile stresses; body fluid/tissue contact; anticipated medical procedures for the patient and environmental elements, e.g., EMI. The Ultra and Ultra 3D families and accessories are suitable and stable in the human body for at least 10 years.

The stability of the Advanced Bionics implants is assured by the materials and processes used in the manufacture of the devices. The implants, including magnets, are carefully designed using materials and processing methods that have a track record of safe, long-term use in implantable devices.

Platinum, used in all Advanced Bionics implants for the stimulation contacts, has been used and accepted as a contact material for long-term stimulation in active implantable devices for over 40 years. For example, Advanced Bionics has used this material in previous implants, some of which have remained implanted in patients since 1994.
Silicone rubber is used to encapsulate the device. The medical device industry has been using silicone rubber in implantable devices since the late 1940s and with a surge in applications starting in the 1960s. The silicone materials used in the manufacture of the currently marketed Advanced Bionics implants are provided by a supplier that specializes in the formulation and manufacture of implantable silicones. Advanced Bionics has used this material in multiple implant products, with no issues related to the stability of this material.

Titanium is used for the electronics housing and the magnet case because of its biocompatibility. Titanium is non-toxic even in large doses and does not play any natural role inside the human body. Titanium is used in a gamut of medical implants, such as hip joint replacement and dental implants that can stay in place for over 30 years. Among metals, titanium benefits from a lower stiffness to more closely match that of the bone, and can more evenly distribute mechanical load. Titanium's chemical resistance stems from its tendency to form a very stable oxide (Ti02) on the surface. Titanium oxide is a common white pigment used in sunscreens, toothpaste, paints, and plastics.

- **Evaluation of clinical data**

Cumulative Survival Rate analysis reporting shows survival rates of over 99% for the currently marketed Ultra implant and Ultra 3D implant.

The post market data including reliability, complaint, adverse events and CAPA data indicated that performance is consistently monitored using the various monitoring tools. Once identified the events are thoroughly investigated, analyzed for root causes and the necessary actions taken to mitigate any risks.

The literature reviews performed examined general, indication, MRI consolidated and headpiece factors. These were conducted according to the state of the art methodology and identified a large amount of published literature. The benefits underline the substantial benefits of cochlear implantation when applied to selected candidates having severe to profound sensorineural hearing loss.

These considerations indicate that the Ultra and Ultra 3D implant systems have a positive risk/benefit profile and hence are suitable for clinical application. The data available from the risk analysis, the literature reviews, standards compliance, and data on long-term reliability all indicate that the products perform well in comparison to other cochlear implant and accessories that are already on the market.

Results of the weighted evaluation of clinical data confirms the continued clinical safety and clinical performance of the products under evaluation. The literature assessments also demonstrate a well characterized safety profile among all products in the Ultra X families. Cumulatively, the above cited evidence supports the clinical safety and performance of the Ultra X systems for restoring a level of auditory sensation in individuals with sensorineural hearing loss.

4.0 Risks and benefits of the investigational device and clinical investigation

- **Anticipated clinical benefits**

The HiResolution Bionic Ear System is intended to restore a level of auditory sensation to individuals with severe-to-profound sensorineural hearing loss via electrical stimulation of the auditory nerve.

- **Anticipated adverse device effects**

Implant recipients incur the normal risks of surgery and general anesthesia. Major ear surgery may result in numbness, swelling or discomfort about the ear, disturbance of taste or balance, or neck pain. If these events occur, they are usually temporary and subside within a few weeks of surgery. Rarely, cochlear implantation may cause a leak of the inner ear fluid, which increases the risk for meningitis. During the surgery, it is a rare possibility that the facial nerve could be injured resulting in a temporary or permanent weakening or full paralysis on the same side of the face as the implant. During the surgery, there is a rare possibility that cerebrospinal fluid leakage or perilymph fluid leakage could occur. As a result of the surgery, it is possible that dizziness, tinnitus, or vertigo may result. If these events occur, they are usually temporary and subside over time. The presence of a foreign body may cause irritation, inflammation, or skin breakdown and may require additional medical treatment or removal of the internal device. Skin infection in the area of the implant may require additional medical treatment or removal of the internal device. There is a possibility that the electrode or device may migrate requiring additional medical treatment or removal of the internal device to address any resulting injury.

- **Residual risks**

Adults who are considering a cochlear implant should be advised of the risk of meningitis. They should also be informed of the availability of vaccines that have been shown to substantially reduce the incidence of meningitis in the general population resulting from the organisms that commonly cause bacterial meningitis (Streptococcus pneumoniae, Haemophilus influenzae).
Extreme direct pressure on the implanted device, up, down, left or right may cause the implant to move and possibly dislodge the electrode array.
A direct impact to the implant site may damage the implant and result in its failure to function. In all cases, the failed device was explanted and a new device reimplanted with no further complications.
The long term effects of chronic electrical stimulation are unknown. Clinical experience with the system has shown no adverse effects of chronic electrical stimulation on recipient performance, electrical thresholds, or dynamic range for almost 30 years.
Electrode displacement can occur if the electrode is not inserted properly. Surgeons should be proficient in the use of the electrode insertion tool. Failure to follow the recommended surgical procedure for placement and stabilization of the Ultra X increases the risk of device migration or extrusion, and of damage resulting from impact trauma, including breakage of the electrode lead wires. Creating a recessed bed for the implant and securely stabilizing the device in place are critical elements of the surgical procedure.
Insertion of a cochlear implant electrode will likely result in a decrease of any residual hearing in the implanted ear.

- **Risks associated with participation in the clinical investigation**

There are no additional risks associated with the participation in this clinical studies than the already known anticipated adverse device effects and residual risks as described above.

- **Possible interactions with concomitant medical treatments**

In general, external components (e.g. sound processor and headpiece) should be removed or deactivated before undergoing the following medical procedures, where the implant may be exposed to electric fields or electrical current. If unexpected sounds or interruptions are experienced during or after medical procedures notify the physician.

- Electrosurgical instruments and RF Ablation instruments are capable of producing radio-frequency voltages of such magnitude that a direct coupling might occur between the cautery tip and the electrode. Induced currents may cause damage to the cochlear tissues or permanent damage to implants. Monopolar electrosurgery and RF Ablation must only be used outside the head or neck region. For the use of bipolar electrosurgical equipment, the probe tips must not contact the implant and should be kept more than 1 mm (.04 in) from the implant.
- Extracorporeal Electrical Stimulation: Electrodes or probe tips used in extracorporeal electrical stimulation instruments such as TENS, TEMS, etc. must not be placed over the implant.
- Neurostimulation: Do not use neurostimulation directly over the implant. High currents induced into the electrode lead can cause tissue damage or permanent damage to the implant.
- Therapeutic Diathermy: Therapeutic diathermy may induce currents in the electrode, which could cause injury to cochlear tissues. The HiRes Ultra X cochlear implants is safe to use during exposure to shortwave (f = 27.12 MHz and E-field = 1.16 kV/m; M-field = 8.5 A/m) and longwave (f = 1 MHz and E-field = 750 V/m; M-field = 2.0 A/m) diathermy.
- Ultrasound: Diagnostic ultrasound can be used anywhere within the following parameters: Power: 1500 mW/cm2, Frequency Range: 3.325 - 3.675 MHz, Duty Cycle: 20%. Therapeutic ultrasound energy must not be used over the implant since it may cause permanent damage to the implant by inadvertently concentrating the ultrasonic field and may cause injury in tissue surrounding the implant.
- Electroconvulsive Therapy: Electroconvulsive therapy must never be used on a cochlear implant patient. Electroconvulsive therapy may cause tissue damage to the cochlea or permanent damage to the implant.
- Ionizing Radiation Therapy: The implant remained functional after being exposed to a total dosage of 250 Gray using a 15 MeV beam strength and 3 cm depth. Ionizing radiation therapy may damage the device. Long term effects of ionizing radiation on the implant may not be immediately detectable. The implant should not be placed directly in the ionizing radiation beam to minimize the risk of tissue necrosis. Diagnostic radiation imaging such as, CT, X-Ray, Mammography, etc. are safe to use.
- MRI Warning:
  For information regarding the use of an MRI scanner with a HiRes Ultra or a HiRes Ultra 3D device, please see the two MRI Safety Information in the appendix.

- **Risk mitigation**

Following the risk analysis risks are mitigated by design, inspections and tests of each specific implant and training. All risks have been reduced to the greatest extent possible. Economic

factors were not considered when determining whether to reduce any risk to the greatest extent possible.

- **Risk-to-benefit rationale**

An overall risk benefit analysis was performed on the Ultra X. There are no unacceptable residual risks associated with the implant.
The overall residual risk remains acceptable when weighed against the benefit of providing sound and speech perception to patients with severe to profound sensorineural hearing loss.

5.0 Objectives and hypotheses of the clinical investigation

- **Primary and secondary Objective**

The primary efficacy objective is to demonstrate that mean Freiburger monosyllabic word score with the Ultra X used in combination with a sound processor (e.g Naida CI) programmed with the latest fitting software (e.g SoundWave 3.2) is at least 20% better than the mean word score at baseline with conventional amplification in the same ear.
The secondary efficacy objective is to demonstrate that mean sentence score (OlSa test) in noise with the Ultra X used in combination with a sound processor (e.g Naida CI) programmed with the latest fitting software (e.g SoundWave 3.2) is equal or higher than sentence score at baseline with conventional amplification in the same ear.

- **Hypotheses**

The primary efficacy hypothesis is

$$\frac{\sum_{ID=1}^{n} word\ score_{6\ months} - word\ score_{baseline}}{n} \geq 20\%$$

with the total number of subject *n*, score (percentage of words correctly understood) in the Freiburger monosyllabic word test with conventional amplification at baseline $word\ score_{baseline}$, score in the Freiburger monosyllabic word test 6 months after device activation $word\ score_{6\ months}$.

The secondary efficacy hypothesis is

$$\frac{\sum_{ID=1}^{n} sentence\ score_{6\ months} - sentence\ score_{baseline}}{n} \geq 0\%$$

with the total number of subject *n*, score (percentage of words correctly understood) in the Oldenburger sentence test with conventional amplification at baseline $senentence\ score_{baseline}$, score in the Oldenburger sentence test 6 months after device activation $sentence\ score_{6\ months}$.

The primary safety hypothesis is that until the appointment six months after device activation not more than one adverse event will occur which require device replacement.

- **Description of the Claims and intended performance of the investigational device**

The HiResolution Bionic Ear System is intended to restore a level of auditory sensation to individuals with severe-to-profound sensorineural hearing loss via electrical stimulation of the auditory nerve.

6.0 Design of the clinical investigation

6.1 General

- **Description of the type of clinical investigation to be performed**

This is a prospective study designed to evaluated the safety and performance of the Ultra X with respective sound processor programmed with the related fitting software under normal conditions of use as it is approved for these devices.

- **Description of the measures to be taken to minimize or avoid bias, including randomization and blinding/masking.**

To minimize the effect of subject-specific factors such as age, cognitive capabilities or etiology of hearing impairment on the investigation outcomes, a study design with within-subject comparisons was chosen. Factors such as gender or lifestyle are not expected to have an effect on study outcomes.

- **Description of the primary and secondary endpoints**

Primary endpoint is the mean Freiburger monosyllabic word score with the Ultra X six months following device activation. It is the aim to demonstrate that six months post activation the group mean Freiburger monosyllabic word score is at least 20% higher than the group mean score at baseline with conventional amplification in the same ear.

The secondary efficacy endpoint is the group mean score in the Oldenburger sentence test in noise six months after device activation compared to the group mean score at baseline in the same ear. Only subjects who achieve less than 75% in the OlSa in quiet will be taken into account, as subjects with poorer performance may not be able to conduct the OlSa in noise with meaningful result (Hey et al., 2014)The group mean score six months after device activation is expected to be at least as good as at baseline.

Testing of both primary and secondary endpoints is described under section 7.0 Statistical considerations.

The primary safety endpoint is a maximum of one device failure that require device replacement during the first six months following device activation (approximately one to eight weeks after surgery).

- **Methods and timing for assessing, recording, and analysing variables**

Visit	Standard Procedure	Study-Related Procedure
Baseline	• Audiological history • Possibly* radiological scan • Freiburger monosyllabic word test • Pure tone audiogram	Depending on center`s standard practice following evaluations may be additionally: • Oldenburger sentence test in noise • Tinnitus and vertigo assessment
Clinic admission with surgery	• Standard surgical and post-surgical procedures • Possibly* radiological scan	• Surgical questionnaire after implantation
Initial device activation (approximately 1-8 weeks after surgery) with rehabilitation[1]	• Initial device activation • Further program optimization • Hearing training	• Questionnaire for the audiologist assessing her/his experience during patient counselling and programming • Audiogram • Tinnitus and vertigo assessment
3 months after device activation (window + ≤ 14 working days)	• Program optimization • Freiburger monosyllabic word test	• Questionnaire for the audiologist assessing her/his experience during patient counselling and programming • Questionnaire for the patient assessing her/his experience at home Depending on center`s standard practice following evaluations may be additionally: • Audiogram • Oldenburger sentence test in noise • Tinnitus and vertigo assessment
6 months after device activation (primary efficacy endpoint) (window + ≤ 14 working days)	• Program optimization • Freiburger monosyllabic word test	• Questionnaire for the audiologist assessing her/his experience during patient counselling and programming • Questionnaire for the patient assessing her/his experience at home Depending on center`s standard practice following evaluations may be additionally: • Audiogram • Oldenburger sentence test in noise • Tinnitus and vertigo assessment
Other	• Unscheduled visits at subject´s or physician´s initiative	• Documentation as unscheduled visit in the respective CRF

Table 2 Summary of standard of care and study related visits and procedures.
** if part of standard hospital practice, not specifically requested in the CIP; sponsor will not receive any scans unless required for AE tracking*

- **Equipment to be used for assessing the clinical investigation variables**

For assessment of feedback from the surgeons or patients questionnaires will be used which were developed specifically for this study. Ratings will be assessed using a 10 point rating scale where 5.5 indicates a neutral rating.

To obtain hearing thresholds and speech perception scores in the Freiburger monosyllabic word test or the Oldenburger sentence test clinics will be using a standard audiometer where the respective tests will be implemented.

- **Description of procedures for the replacement of subjects**

Subjects who withdraw or who are discontinued prior to the completion of the six-months follow-up visit will be replaced. Unless withdrawal of consent all data as per protocol will be gathered and used in the analysis. Thus the total enrollment may exceed 30 so that a total of 30 subjects will provide valid and complete data sets. Subjects who withdraw or who are discontinued from the study will be reported on the appropriate Case Report Form. These subjects will continue to receive standard clinical care and keep the implant.

The Investigator (or authorized delegate) in cooperation with the trial monitor will complete a log to document the disposition of each enrolled subject (completed study, withdrew, discontinued).

6.2 Investigational device(s) and comparator(s)

- **Description of the exposure to the investigational device(s) or comparator(s)**

The investigational device is implanted surgically under the skin behind the ear. The internal receiver includes of HiRes™ Ultra Cl HiFocus™ MS Electrode and HiRes™ Ultra 3D Cl HiFocus™ MS Electrode that are implanted surgically under the skin behind the ear. The electrode array has 16 contacts which are connected to the implant through the electrode lead. The receiver stimulator encapsulates the electronics into a titanium casing, the antenna coil allows for forward and backward telemetry between the implant and the external parts. The antenna coil also includes a magnet in order to retain the external headpiece.

The external components include a sound processor (body-worn or ear-level), a headpiece, and a cable. The system converts sound into electrical energy that activates the auditory nerve. The auditory nerve then sends information to the brain, where it is interpreted as sound.

- **Justification of the choice of comparator(s)**

There is no comparator device in this study; data will be analyzed as within-subject comparison, therefore a comparator is not needed.

- **List of any other medical device or medication to be used during the clinical investigation**

This study protocol follows very closely the standard clinical care. There is no additional medical device or medication needed which would not be needed in standard clinical care.

- **Number of investigational devices to be used, together with a justification**

Each subject will receive one implant; therefore we plan 30 implants for this study, but it may be more if a subject needs to be replaced (see above Description of procedures for the replacement of subjects)

6.3 Subjects

- **Inclusion criteria for subject selection**
  - No previous experience with any auditory implant
  - 18 years of age or older
  - Postlingual onset of severe hearing loss (≥ 4 years of age)
  - Limited benefit from appropriately fitted hearing aids, defined as scoring 60% or less in Freiburger Monosyllabic word test (either assessed by a previous hearing aid experience or the audiologist`s judgment based on pure tone thresholds in case of profound deafness)
  - German language proficiency
  - Willingness to participate in all scheduled procedures outlined in the protocol

- **Exclusion criteria for subject selection**
  - Cochlear malformation or obstruction that would preclude full insertion of electrode array.
  - Presence of disabilities other than deafness that would prevent or interfere with participation in the required study procedures
  - Medical or psychological conditions that contraindicate surgery or impact the ability to manage an implanted device or the study related procedures
  - Evidence of central auditory lesion or compromised auditory nerve
  - Pregnancy at time of surgery.

- **Criteria and procedures for subject withdrawal or discontinuation**

Subjects may withdraw from the study at any time, with or without reason, and without affecting continued standard of medical care they would receive. Subjects can be discontinued from the study for the following reasons:

- Withdrawal of consent
- A safety concern noted by a clinician that endangers the subject or cannot be tolerated for medical and/or ethical reasons
- Inability of the subject to perform the tasks necessary to provide usable data for the study.
- Failure to attend a follow-up visit after three documented attempts to contact the subject and reschedule the visit.

- **Point of enrolment**

An individual is considered to be enrolled as a study subject only after the Informed Consent Form (ICF) has been signed. Each subject will get ample time to consider participation in the trial. Once enrolled, the subject will be assigned a unique identifier. The identifier will consist of an alphanumeric sequence that will consist of the investigational site identifier and the sequential subject number.

- **Total expected duration of the clinical investigation**

In total, the clinical investigation will run for 24 months.

- **Expected duration of each subject's participation**

Each subject's participation in the clinical investigation will last approximately 10 months (consent, baseline data, surgery up to 10 weeks later, initial device activation 4 to 8 weeks after surgery, 6 months follow-up period).

- **Number of subjects required to be included in the clinical investigation**

Complete data sets of 30 subjects will be required. The total number of subjects enrolled may be higher in case a subject needs to be replaced due to withdrawal or discontinued follow up.

- **Estimated time needed to select this number (i.e. enrolment period)**

It is planned to enroll three to five centers in Germany. Selection and enrolment of the clinics may take up to 6 months. Once a clinic is prepared to start the study and has all required approvals in place we estimate an additional 10 months for enrollment of a minimum of 5 subjects. This results in an overall estimated time for enrolment of 12 months.

6.4 Procedures

- **Description of all the clinical-investigation-related procedures for the subjects**

No investigational procedures outside of the clinical routine are used to screen subjects for study eligibility. Subjects eligible to participate in this study already will have been evaluated and considered to have met the surgical and audiological criteria for cochlear implantation. Cochlear implant eligibility will be determined using standard-of-care tests and procedures. These tests may include radiographic imaging to assess cochlear patency, audiometric hearing thresholds, and speech/auditory perception tests.
All study visits are summarized in table 2. The time window for the post-operative visits is + ≤ 14 working days. This time window is chosen because it allows a sufficient amount of time for subjects to find a date that fits their agenda for the follow ups to be performed. The medical history will include demographic information (gender, date of birth, etiology of hearing loss and hearing aid use) and otology history that might impact study outcomes (chronic ear infections, ear surgeries, history of tinnitus or vestibular disturbances).
Hearing test results obtained prior to enrollment may be used as baseline data if the results were obtained no more than 10 weeks prior to surgery.
Unscheduled visits to the implant center may be made at any time for evaluation of possible adverse events or to address any questions or concerns expressed by the subject that cannot be managed adequately by telephone or e-mail.
After the study visits are completed, subjects will continue to receive standard medical routine treatment.
The participating surgeons will be asked after each surgery about details of their surgical technique, for example how the access to the middle ear was configured and how the implant was secured. These details allow to assess how the fantail area of the implant was treated during the surgery and how it is supported once positioned in its final position.
Further the audiologist will receive a questionnaire to assess his experience when using the fitting software and when explaining the system to the patient.

Measurement procedures:

Pure Tone Audiogram

For the pure tone audiogram thresholds will be measured with a clinical audiometer.
Conditions: At baseline thresholds will be measured unaided with headphones or insert earphones for each side separately as well as with bone conduction. Further the aided thresholds shall be determined for each side separately. After surgery threshold will be measured in free field using the processor in its normally used setting.
For acoustic stimulation thresholds shall be determined at the frequencies 125, 250, 500, 1000, 2000, 4000 and 8000 Hz; for bone conduction the frequencies 250, 500, 1000, 2000 and 4000Hz shall be measured.

Freiburger Monosyllabic Word Test

The Freiburger Monosyllabic Word Test will be conducted with a clinical audiometer. The signal will be presented at 65dB from a loudspeaker in front of the subject. The score will be obtained as the percentage of words correctly understood.
In each condition two lists shall be tested. During the study lists shall not be repeated.
Conditions: At baseline the monosyllabic word test will be conducted in free field on the ear to be implanted. The patient shall use the hearing aid setting with which he obtains best results. The score obtain is the baseline monosyllabic word score. With the CI system the monosyllabic word test will be measured in free field using the processor in its normally used setting.

Oldenburger Sentence Test (OlSa)

The Oldenburger Sentence Test will be performed in an adaptive way using a clinical audiometer. Both, signal and noise, shall be presented from the loudspeaker in front of the subject. The noise will be presented at 65dB in a continuous way. The signal will be varied to obtain the signal-to-noise ratio at which the patient will correctly understand 50% of the words. This is called speech reception threshold (SRT) measured in dB.
Prior to collecting results for the study subjects shall pass a training. Typically the training consists of four lists of the OlSa in quiet. The training may be adapted based on the individual needs to be shorter or longer. For the study relevant data in each condition two lists shall be tested and each list shall have 30 sentences. During the study lists shall not be repeated.
Some subjects may not be able to pass the OlSa in noise successfully. The OlSa does not converge for subjects with too poor performance. In order to avoid frustration and spending time inappropriately only subjects with a certain speech understanding in quiet will be required to conduct the OlSa in noise. Therefore the OlSa in quiet shall be conducted first. The signal shall be presented from the front at 65dB and words understood correctly shall be counted. Subjects who achieve less than 60% do not need to conduct the OlSa in noise as clinical experience shows that these subjects are not able at all to pass the OlSa in noise.
Hey et al., 2014 set the criteria at 75% in the OlSa in quiet. Therefore the secondary objective will only respect subject with 75% or more. But as a test in quiet reflects different abilities than a test in noise the test in quiet is only a rough estimator. Hey at al. did not investigate subjects below 75%. Therefore subjects between 60% and 75% in quiet shall pass the OlSa in noise as supportive data. In case the audiologists estimates that the whole test session may be too exhausting for the subject and may therefore not give valuable results she or he may decide to use either two OlSa lists with 20 sentences, or only one list with 30 sentences. She or he will

select the option which seems more appropriate in the specific situation. The decision will be documented in the CRF.

Conditions: At baseline the Olsa will be conducted in free field on the ear to be implanted. The patient shall use the hearing aid setting with which he obtains best results. The SRT obtained in this condition is the baseline SRT. With the CI system the OlSa will be measured in free field using the processor in its normally used setting .

Surgeon`s questionnaire:
The surgeon will receive a paper based questionnaire in which she/he will be asked to report her/his experiences during the surgery. For questions requiring a rating a 10 point scale will be used. The data will then be entered to the eCRF data base and monitored.

Audiologist`s questionnaire:
The audiologist will receive a questionnaire in which she/he will be asked to report her/his experiences during the fitting an counselling. This questionnaire will be realized in the eCRF data base. For questions requiring a rating a 10 point scale will be used.

Patient`s questionnaire:
The patient will receive a questionnaire in which she/he will be asked to report her/his experiences with the CI system. This questionnaire will be realized with an ePRO module in the eCRF data base. For questions requiring a rating a 10 point scale will be used. In case the patient needs any help to fill in the questionnaire, the audiologist may support him.

Data obtained in the fitting process:
When starting the fitting the fitting software will at first measure the impedances of intra-cochlear electrode contacts. Further the audiologist will determine several parameters in the fitting process. Especially the M-level will be of interest.
During standalone operation of the CI system the processor logs the duration of use in classified environments. When connected next time to the fitting software these data will be downloaded and are available for further evaluation.

- **Description of those activities performed by sponsor representatives**

The sponsor will provide the general training required for using the medical devices (Ultra X with all accessories and tools, processor and fitting software) in standard clinical care. Further the sponsor will take care of all study specific training, such as training on the study schedule and study specific procedures. Data management, data evaluation and potentially a draft for a scientific publication will be provided by the sponsor.

- **Any known or foreseeable factors that may compromise the outcome of the clinical investigation or the interpretation of results**

In the study design each subject serves as his own control. This carries the risk of changes in the general condition of a subject which cannot be reflected in the baseline measurements. Even though the duration of the study is relatively short other factors may influence the results, such as any additional illness. Still this seems to be the best study design and the risk is mitigated by

the fact that only approximately 10 months will be observed and the sample size is higher than required for the efficacy objective.

6.5 Monitoring plan

A clinical research monitor will supervise conduct of the study at each site. The monitor will visit the Investigator and the study facility at periodic intervals in addition to maintaining ongoing telephone, e-mail, and/or letter contact. The monitor will maintain up-to-date personal knowledge of the study through observation, review of study records and source documentation, and discussion of the study with the Investigator and study personnel.

The Sponsor's internal auditors or contract auditors may evaluate the conduct of the study at a site. These parties will have access to all study-related documents. The Sponsor audit reports are confidential and proprietary.

All investigators and investigational sites will be monitored on a continuing basis through the course of the clinical study to oversee compliance with the regulatory and clinical aspects of the study. A Clinical Monitor will maintain current personal knowledge of the study through observation, review of study records and source documentation, and discuss and update study related issued with the investigators and study site staff.

The following information is reviewed and discussed during site initiation training:

- Good Clinical Practice, including investigator responsibilities and purpose of monitoring activities
- Requirements for EC approval (initial application and continuing reviews)
- Informed consent procedures, including requirements for inclusion of all foreseeable risks in the ICF
- Study protocol and procedures
- Processes for recording and reporting adverse events
- Device accountability procedures
- Data collection and correction procedures, source documentation, and record retention requirements

NOTE A detailed plan for monitoring arrangements will be prepared separately from the CIP.

6.5.1 Pre-Study Documentation Requirements

Prior to obtaining consent from any subjects, the following documents must be provided to Advanced Bionics:

- A copy of the protocol signature page and investigator agreement, signed and dated by the Principal Investigator and Co-Principal Investigator(s), if applicable
- A signed and dated copy of the Clinical Study Agreement
- A copy of the written EC approval of the protocol
- A copy of the approved ICF and written EC approval of the form
- A copy of the curriculum vitae of the Principal Investigator and Co-Investigator(s), if applicable

- Financial disclosure forms

6.5.2 Study Documentation/Case Report Forms

Data must be submitted according to protocol requirements for all enrolled subjects. CRFs provided for this study must be used to submit data to the Sponsor. Each subject will be assigned a unique identifier at the time of enrollment (as described above), which will be used on all CRFs.

Study records are comprised of monitored CRFs, and all other administrative documents including, for example, EC correspondence, clinical trial materials and supplies shipment manifests, monitoring logs, and correspondence with the Sponsor. A study-specific binder will be provided with instructions for maintenance of study records.

Source documentation is defined as any hand-written or computer-generated document that contains medical information or test results that have been collected for or are in support of the protocol specifications. For example, these documents may include audiograms, results from CT scans and x-rays, lab reports, clinic notes, subject questionnaires, and telephone logs. All draft, preliminary, and pre-final versions of a report also are considered source documents, including faxed reports or data and hard copies of test results.

6.6 Interim Monitoring Activities

The Clinical Monitor will perform at least the following activities during on-site visits:

- Confirm that the facilities continue to be appropriate and that the study records are stored in a secure location
- Conduct review and collection of regulatory documents
- Review subject ICFs for completeness and accuracy
- Confirm that the study protocol is being followed and that any changes in the protocol have been reported to the EC and Advanced Bionics, as applicable
- Review CRFs and source documents for completeness, accuracy, and timely submission to the Sponsor
- Verify that all adverse events have been reported to the Sponsor within the appropriate timeframe. If an event is discovered that requires reporting, the Clinical Monitor will instruct the investigators to document the event on the appropriate CRF and submit to the Sponsor within the required timeframe
- Review and resolve data clarification requests, if appropriate
- Review device accountability records
- Follow up on outstanding monitoring visit action items

At the end of the visit, the Clinical Monitor will meet with the investigators to review site compliance with the protocol, investigator responsibilities, and applicable regulations.

6.7 Close-Out Monitoring Activities

The Clinical Monitor performs at least the following activities during study close out:

- Conduct review and collection of regulatory documents
- Resolve open data clarification requests

- Review study file retention and storage requirements
- Collect outstanding CRFs
- Review investigator responsibilities including EC notification of study closure
- Follow up on any outstanding issues, including unresolved adverse events.
- Review post-study financial disclosure requirements
- Review the potential of regulatory or Sponsor audits.

At the end of the visit, the Clinical Monitor will meet with the investigators to review site compliance with the protocol, investigator responsibilities, and applicable regulations.

6.8 Management of Site Noncompliance

Noncompliance with the signed agreement, the CIP, regulatory requirements, or any conditions of approval imposed by the EC will be addressed by re-training the investigators on the appropriate study procedures and documenting the re-training. Continued noncompliance may result in termination of study participation.
In the event of site termination and the use of investigational product, the Sponsor will stop shipping investigational product and request that any investigational product at the site be returned.

6.9 Documentation and Records

The Sponsor and investigators maintain files with Ethical committee and regulatory documents. CRFs are completed for each study subject. The Sponsor maintains the original CRFs and the study site retains copies of all CRFs. The Clinical Monitor documents monitoring activities and prepares a report after each monitoring visit.

All study records (e.g., protocol, correspondence with the Sponsor and the EC, EC approvals, CRFs, subject records, consent forms, reports) must be maintained by the Investigator until notified by the Sponsor and at least as long as local document retention regulations require. If an Investigator opts to discontinue participation in the study, all records will be transferred to a mutually agreed designee (i.e., another Investigator).

This transfer is subject to the Sponsor's approval and will be documented in writing with copies sent to the sponsor. If an Investigator leaves the site at which the study was conducted, the Sponsor should be contacted regarding the disposition of documents.

In the event of an audit, the Investigator agrees to allow representatives of the Sponsor or other regulatory authorities to access all study records. The Investigator will notify the Sponsor promptly of all audit requests from government or other regulatory agencies and will promptly forward a copy of all audit findings to the Sponsor.

6.10 Compensation

The clinical site will be compensated for their time and effort to fulfil the obligations of this clinical study. Study subjects will be compensated for their travel expenses in case they need to visit the site due to a study visit outside of the clinical routine.

7.0 Statistical considerations

- **Statistical design, method and analytical procedures**

The hypothesis is that the mean Freiburger Monosyllabic words score will be at least 20% better six months after device activation compared to baseline with conventional amplification in the same ear.
The secondary efficacy endpoint is the mean Oldenburger sentence test score six months after device activation compared to conventional amplification baseline performance in the same ear. If the primary efficacy analysis proves statistically significant, then the results will be analyzed for the secondary endpoints using a non-inferiority hypothesis.

- **Sample size, level of significance and power of the investigation**

A total sample size of 30 subjects is planned for this study based on efficacy and safety considerations.

In order to estimate the required sample size to demonstrate safety and efficacy of the device, both the primary efficacy endpoint as well as the primary safety endpoint were taken into account.

In order to estimate the standard deviation of Freiburger Monosyllabics 6 months after first fitting the following sources were considered:
1) the "Safety and efficacy trial of the HiFocus™ mid-scala electrode array" (sponsored by AB in 2012/13): In that study speech perception was measured with a word test in quiet a) with a hearing aid on the ear to be implanted prior surgery as well as b) with the CI on the same ear three months after device activation. A mean improvement of 49.5% with a standard deviation of 22% was found.
2) Data from an evaluation of postoperative speech performance conducted by the Unfallkrankenhaus Berlin (Battmer et al., in press): the evaluation included only subjects with a pre-operative score in Monosyllabics of 0%. At three months after device activation subjects reached a score of 54% with a standard deviation of 24%.
3) The publication from Helbig et al. (2014): this publication analyses preservation of residual hearing after cochlear implantation. Prior surgery subjects had a mean score in the Monosyllabic word test of 16% and six months after device activation the group reached 61% with a standard deviation of 24% (derived from fig. 4B).
4) The publication from Lenarz et al. (2011): in a retrospective analysis the effect of technological advances in the past 20 years on the hearing performance was determined. For subjects with recent CI systems a three months word score of 48.3% with a standard deviation of 29.0% was reported. Mean score at six months after device activation can only be estimated from the diagram, it is about 54% with no standard deviation mentioned in the paper.

Supposedly the standard deviation is not significantly different three or six months after activation; we therefore assume a standard deviation б=25% for the sample size calculation. Sample size calculation was performed using G*Power 3.1.9.4 (Faul et al., 2007). The expected difference Δμ=20% was derived from the "White Book for Cochlear Implantation" of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (Weißbuch Cochlea-Implantat(CI)-Versorgung, DGHNO, 2018). This yields to a standardized difference in means of dz = Δμ/ б = 0.8. The number of subjects required to demonstrate an equivalent improvement at a type-1 error rate of α=0.025 and a power 95% was determined to be 24.

The sample size was expanded to 30 in order to provide sufficient data for determining the safety and reliability of the electrode. AB internal data reveal a cumulative survival rate of 99.93% for the Ultra 3D, 99.98% for the Ultra and 99.92% for the Advantage (the predecessor of the Ultra). This survival rate included all types of failures needing device replacement. So the probability of experiencing a device failure during the first 3 months is <0.08 %. The probability of observing at least one failure requiring device replacement in a sample size of 30 is 2.4%, and accordingly, one event may occur in a sample of 30.
Based on these considerations we concluded that a target number of 30 subjects enrolled in the study will be sufficient to allow the conclusion that the confirmatory data represents valid information.

- **Expected drop-out rates**

Experience so far has shown that the drop-out rate in this kind of investigation is very low, as the appointment coincide with the regular clinical follow-up intervals. We expect that maximally two subjects drop out from the investigation. Any drop-out will be replaced.

- **Pass/fail criteria to be applied to the results of the clinical investigation**

Primary efficacy and safety objectives need to be fulfilled in order to successfully close the study.

- **The provision for an interim analysis, where applicable**

Results will be analyzed on an annual basis.

- **Criteria for the termination of the clinical investigation on statistical grounds**

It is not planned to terminate the investigation on statistical grounds.

- **Procedures for reporting any deviation(s) from the original statistical plan**

In case of an deviation from the statistical plan, the annual report will highlight and justify the deviations.

- **Specification of subgroups for analysis**

No sub-group analysis is planned.

- **Procedures that take into account all the data**

The annual analysis will take all data into account.

- **Treatment of missing, unused or spurious data, including drop-outs and withdrawals**

Subject who withdraw from the study will be replaced. Therefore we do not expect any missing data for the primary endpoint. If still any data are missing, an analysis will be conducted using the observed results. A further analysis also will be completed that imputes 0 for the change from baseline for non-completers. In that case, the imputation analysis would become the primary efficacy evaluation.

- **Exclusion of particular information from the testing of the hypothesis, if relevant**

This is not planned.

- **Minimum and maximum number of subjects to be included for each centre in multicentre clinical investigations**

It is expected that each participating center enrolls 3 to 8 subjects.

8.0 Data management

- **Procedures used for data review, database cleaning, and issuing and resolving data queries**

An electronic Case Report Form (eCRF) data base will be used. The system allows to track all entries, queries and changes. Data will be verified according to the monitoring plan. Further, in case of outliers source data will be checked. Data will be exported for further analysis, e. g. in Excel or Statistica.

- **Procedures for verification, validation and securing of electronic clinical data systems, if applicable**

The eCRF data base will be validated following AB´s QMS procedures. The eCRF system is provided by IBM, who takes care of securing the data system.

- **Procedures for data retention**

eCRFs will be used to collect all subject data during the study. eCRFs must be fully completed for each subject and electronically signed. They will be available for the Clinical Monitor who will work under ICH-GCP rule.
The investigators or the authorized study personnel are required to electronically sign the eCRF pages where needed to validate they have read and are in agreement with the reported data.

- The investigator or designated individual is responsible for recording all data from the trial on the eCRFs supplied by the Sponsor. The data reported in the eCRF must be unambiguous.
- Implementation of the eCRF data base will be performed by the Sponsor.

By signing the study protocol, the investigator agrees to keep all information made available to him/her in strict confidence and ensures the same level of confidentiality from his/her staff. The information made available to study hospital personnel must not be passed on to others without written authorization of the Sponsor.

- **Specified retention period**

Study documents (study protocol, CRFs and other materials) made available by/to the principal investigators need to be stored adequately in order to assure their confidentiality in the hospital for a duration of 15 years.

- **Other aspects of clinical quality assurance, as appropriate**

The Investigator will assure proper implementation and conduct of the study including those study-related duties delegated to other appropriately qualified individuals and designated in the study documentation. The Investigator will assure that study personnel cooperate with monitoring and audits, and will demonstrate due diligence in recruiting and retaining study subjects.

9.0 Amendments to the CIP

- **Description of the procedures to amend the CIP**

The protocol must be followed exactly. Any changes to the protocol must be implemented through a formal protocol amendment. Amendments to the protocol must be initiated by the Sponsor or at the request of other parties. In either case, a formal amendment cannot be initiated until it has been approved by the Sponsor, the Investigator, regulatory agencies (if applicable), and the EC. It can only be altered by written approved amendments by the Clinical Project Manager (CPM). Administrative changes that do not affect the subject risk ratio may be made after consulting AB AG.

10.0 Deviations from clinical investigation plan

- **Statement specifying that the investigator is not allowed to deviate from the CIP, except as specified in ISO 14155:2011 4.5.4**

The Investigator must agree that the study will be conducted according to this CIP, the principles of ISO 14155:2011, 90/385/EEC, ICH-GCP, Declaration of Helsinki and internal Standard Operating Procedures (SOPs) and local regulations.

- **Procedures for recording, reporting and analysing CIP deviations**

Deviations from the clinical protocol and protocol requirements including GCP and ISO14155:2011 guidelines will be reviewed and evaluated at each monitoring visit.
A very serious deviation that affects the scientific soundness of the study or any aspect of the subject's safety, rights or wellbeing may be a cause to close the study at an investigational center. In addition, these very serious deviations will require urgent reporting to ECs and data management.

- **Notification requirements and time frames**

The requests for deviations, and reports of deviations, if the deviation affects subject's rights, safety and wellbeing, or the scientific integrity of the clinical investigation shall be provided to the EC.
Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of human subjects may proceed without prior approval of the sponsor and the EC. Such deviations shall be documented and reported to the sponsor and the EC as soon as possible.

- **Corrective and preventive actions and principal investigator disqualification criteria**

Appropriate corrective actions will be implemented as necessary. Each and every deviation from the protocol requirements and European standard ISO 14155:2011 'clinical investigation of medical devices' will have to be reported as 'Protocol Deviation'.

Advanced Bionics AG may disqualify a clinical investigator if the clinical investigator has repeatedly or deliberately failed to comply with applicable regulatory requirements or the clinical investigator has repeatedly or deliberately submitted false information to Advanced Bionics or, if applicable, to any ethics committee in any required report. A disqualified clinical investigator is not eligible to receive investigational devices, and is not eligible to conduct any clinical investigation that supports an application for a research or marketing permit for products.

11.0 Device accountability

- **Description of the procedures for the accountability of investigational devices**

As all the products that are used in this study are commercially available on the CE market no study specific accountability will be performed. Data on which subject was implanted with which implant will be tracked according to standard clinical care. Devices are not labeled differently than those that will be used for subjects who do not participate in the study.

12.0 Statements of compliance

- **Statement specifying that the clinical investigation shall be conducted in accordance with the ethical principles**

This clinical investigation is conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

- **Statement specifying compliance with this International Standard and any regional or national regulations, as appropriate.**

This clinical investigation is conducted in compliance with ISO 14155:2011.

- **Statement specifying that the clinical investigation shall not begin until the required approval/favourable opinion from the EC or regulatory authority have been obtained, if appropriate.**

This clinical investigation will not begin until the required approval/favourable opinion from the center specific EC have been obtained.

- **Statement specifying that any additional requirements imposed by the EC or regulatory authority shall be followed, if appropriate.**

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

- **Statement specifying the type of insurance that shall be provided for subjects, if appropriate.**

Due to the fact that all devices are market approved and used according to the approved indication there is no study specific insurance required according to local regulation.

13.0 Informed consent process

- **Description of the general process for obtaining informed consent**

The Informed Consent Form must be provided to the Sponsor for approval prior to submission to the EC. The Sponsor will provide an informed consent template and assistance in adapting that template to conform to local requirements. Before enrollment, the study will be explained to each prospective study candidate. Candidates will be asked to read the approved ICF and given the opportunity to ask questions. Once all questions have been answered and the Investigator is assured that the individual understands the implications of participating in the study, the subject will be asked to sign the ICF. Each subject must get ample time to consider participation in the trial. The Investigator will provide a copy of the signed ICF to each subject. If an amendment to the protocol changes the scope or activities associated with a subject's participation, or increases the potential risk to the subject, the ICF must be revised and submitted to the EC for review and approval. The revised ICF must be used to obtain consent

from a subject currently enrolled in the study if he or she is affected by the amendment. The revised ICF must be used to obtain consent from any new subject who is enrolled in the study after the date of the approval of the amendment. Any modification of the consent, e.g. subject information made by an investigator has to be authorized by the Sponsor before it is sent to the EC.

- **Description of the informed consent process in circumstances where the subject is unable to give it; in the case of emergency treatment, the items specified in ISO 14155:2011 4.7.3.4 shall be included**

Studies conducted by AB do not involve emergency treatment or any other situation where a subject in unable to give consent.

14.0 Adverse events, adverse device effects and device deficiencies

- **Definitions of adverse events and adverse device effects**

An adverse event (AE) is defined as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (incl. abnormal laboratory findings) in subjects, users or other persons whether or not related to the investigational device.

A *serious adverse event* (SAE) is an event that leads to:

- Death due to any cause
- A life-threatening illness or injury
- A permanent impairment of a body structure or a body function
- In-subject hospitalization or prolongation of existing hospitalization
- Medical or surgical intervention to prevent permanent impairment to body structure or body function
- Fetal distress, fetal death, congenital abnormality or birth defect.

An *adverse device effect* (ADE) is any untoward and unintended response to a medical device.

NOTE 1 This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

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

- **Definition of device deficiencies**

A device deficiency is the occurrence of inadequacy of the medical device with respect to its identity, quality, durability, reliability, safety or performance.

Device deficiencies include malfunctions, use errors, and inadequate labelling.

- **Definitions of serious adverse events and serious adverse device effects and, where appropriate, unanticipated serious adverse device effects**

A *serious adverse device effect* (SADE) is an event that resulted in any of the consequences characteristic of a serious adverse event (SAE) or that might have led to any of the consequences if suitable action had not been taken or interventions had not been made or if circumstances had been less opportune.

An *unanticipated adverse device effect* (UADE) Is any serious adverse effect on health or safety; any life threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
All adverse events and adverse device effects, serious and non-serious and device deficiencies will be tracked during the course of the study using the appropriate case report form. Case report forms should include, but are not limited to:

- Description of event, duration, and severity
- Date that event was first detected (if after surgery)
- Course of action taken
- Status (resolved, improving, no change, worsening). The status of the event will be tracked throughout the study until it is resolved or the study is closed.
- Subject and device identification

The relationship between the study procedures and the incidence of an adverse event will be classified by the investigator in categories as divided in the CRF:

- Not related
- Related
- Unknown

- **Time period in which the principal investigator shall report all adverse events and device deficiencies to the sponsor and, where appropriate, to ECs and the regulatory authority**

Adverse events classified as SAE according to the definition above have to be reported by the investigator to AB AG without unjustified delay but nevertheless within 48 hours after first knowledge of the event. Investigator – AB AG reporting should preferably be done by the eCRF in combination with an e-mail or fax to the address indicated in this CIP. Initial reporting must be concluded within 48hrs of awareness, irrespective of missing data/information. If additional information or documentation is needed, the study manager will be responsible to contact the study center in order to retrieve the necessary information.

- **Details of the process for reporting adverse events (date of the adverse event, treatment, resolution, assessment of both the seriousness and the relationship to the investigational device)**

Evaluation of any SAEs, SADEs, and UADEs will be conducted promptly. Confirmed SAEs, SADEs, and UADEs will be reported by the Sponsor to all ethics committees as soon as possible but in any case within 2 working days after receiving notice of the event. If it is determined that an event or effect presents an unreasonable risk to subjects, this study, or those parts of the study presenting that risk, will be terminated not later than 5 working days after the determination is made and not later than 15 working days after the Sponsor/Clinical Research first received notice of the effect (section 4.7).
All other issues related to the device will be reported to Advanced Bionics AG, as indicated in the product manuals.

As Serious Adverse Events (SAE) and Serious Adverse Device Effects (SADE) are treated identically with respect to the procedures given in this section, the term SAE will include the term SADE in this section.

- **Details of the process for reporting device deficiencies**

In this clinical investigation Adverse Events and device deficiencies will be collected using the applicable section in the Case Report Form based on Adverse Event Report and registered into AB`s vigilance data base, if applicable. AE and ADE will be included in periodic safety reports and in the clinical study report. More immediate and direct reporting to EC and/or NCAs is required when AE or ADE are classified as SAE or USADE.

- **List of foreseeable adverse events and anticipated adverse device effects, together with their likely incidence, mitigation or treatment**

Anticipated adverse device effects and residual risks as well as possible interactions with concomitant medical treatments are described in 4.0 Risks and benefits of the investigational device and clinical investigation.

- **Emergency contact details for reporting serious adverse events and serious adverse device effects**

Emergency deviations or modifications must be reported to the Sponsor and the EC no later than 24 hours after the emergency.
Study Management accepts the right of the investigator to deviate from protocol in a medical emergency when necessary to safeguard the life or physical wellbeing of the subject. The following conditions must apply for a situation to be considered a medical emergency:

- The subject is in a life threatening situation and needs immediate treatment.
- No generally acceptable alternative for treating the subject is available.
- Time does not allow the investigator to notify the Sponsor to obtain regulatory approval.

In these cases the investigator is obliged to notify the CPM immediately who will notify the EC and Regulatory agencies no later than 5 working days after the event was reported.

Emergency Contact for reporting serious adverse events and serious adverse device effects:

Name	[redacted]
Address	Advanced Bionics AG Clinical Research Laubisrütistrasse 28 CH-8712 Stäfa, Switzerland
Telephone	[redacted]
e-mail	[redacted]

- **Information regarding the DMC, if established**

Not applicable

15.0 Vulnerable population

In this PMCF study no vulnerable subjects will be recruited.

16.0 Suspension or premature termination of the clinical investigation

- **Criteria and arrangements for suspension or premature termination of the whole clinical investigation or of the clinical investigation in one or more investigation sites**

AB AG reserves the right to terminate the study or enrolment at any center at any time. However, this right will be exercised only for valid scientific or business reasons (excluding as a reason the actual interim study results), or because of issues related to protection of research subjects.

Possible reasons for suspending or terminating a center include:

- Investigator non-compliance.
- Repeated failure to complete or submit CRFs in a timely manner.
- Failure to obtain written informed consent from each subject.
- Failure to report an SAE or UADE to the Sponsor within the required timeframe.

Investigators and EC s will be notified in writing in the event of termination.

- **Criteria for access to and breaking the blinding/masking code in the case of suspension or premature termination of the clinical investigation, if the clinical investigation involves a blinding/masking technique**

Not applicable for this study.

- **Requirements for subject follow-up after termination**

After termination of this study subjects will continue their standard clinical care.

17.0 Publication policy

- **Statement indicating whether the results of the clinical investigation will be submitted for publication.**

The study may be published on conferences and in a peer reviewed journal. Please consider the details in the contract.

- **Statement indicating the conditions under which the results of the clinical investigation will be offered for publication**

It is planned to publish the study results at conferences as potentially in a peer reviewed journal. Once the evaluation of all data is finished, sponsor and investigator shall discuss the details of the publication (format, journal, authors etc.) The sponsor will not have a veto.

18.0 Bibliography

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Apendix:

A MRI Warning

MRI warning for Ultra
MRI Warning for Ultra 3D

B Questionnaires

Questionnaire for the surgeon
Questionnaire for the audiologist
Questionnaire for the patient

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