Benefits of the HiResolution Bionic Ear System in Adults with Asymmetric Hearing Loss

INVESTIGATIONAL PLAN CR0314
FEASIBILITY IDE

16 August 2017

Advanced Bionics, LLC
28515 Westinghouse Place
Valencia, CA 91355

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1.0 Investigator Signature Page

Study Title:	Benefits of the HiResolution Bionic Ear System in Adults with Asymmetric Hearing Loss
Study Center:	Center Name Address Phone

I have been provided a copy of the following Food and Drug Administration (FDA) regulations: 21 CFR Part 812 – Investigational Device Exemptions; 21 CFR Part 50 – Protection of Human Subjects.

I agree and/or certify that:

1. I will conduct this clinical trial in accordance with this agreement, all requirements of the investigational plan, IDE regulations, other applicable regulations of the FDA, and any conditions imposed by my reviewing Institutional Review Board (IRB). I agree to abide by all of the responsibilities of Investigators addressed under 21 CFR 812, Subpart E and Subpart G.
2. I will ensure that an IRB will be responsible for the initial and continuing review and approval of this clinical trial. I will submit the certification of IRB approval to the sponsor (21 CFR 812.62; 21 CFR 812.42).
3. I will ensure that Informed Consent is obtained from each subject participating in this clinical trial and that a signed and dated copy of the informed consent is available to the sponsor and the sponsor's designated monitor (21 CFR Part 50; 21 CFR 812.150).
4. I will supervise all testing of the investigational device on human subjects and will allow only certain study personnel listed on the delegation log to administer this device and/or perform follow-up evaluations of the device (21 CFR 812.110 c).
5. I will be responsible for accountability (records of receipt, use and disposition) of the investigational device at the study site. I will return all unused investigational product to the sponsor or otherwise follow the instructions of the sponsor for disposal of the unused devices (21 CFR 812.140 a; 21 CFR 812.110 d).
6. I will ensure the accurate completion of case report forms and I will submit completed case report forms, adverse events, withdrawal of IRB approval, deviations, progress reports and a final report to the sponsor at the time frames specified in the Protocol, FDA regulations, and/or local IRB regulations (21 CFR 812.150).
7. I agree to maintain adequate and accurate records and to make those records available for sponsor monitoring or a regulatory inspection (21 CFR 812.140).
8. I will ensure that all associates, colleagues, and employees assisting in the conduct of this trial are informed about their obligations in meeting the commitments on this agreement (21 CFR 812.100).

9. I have the appropriate, relevant qualifications to conduct and to oversee the conduct of the clinical trial as documented on my curriculum vitae (21 CFR 812.43).
10. I will disclose sufficient and accurate financial information to sponsor by completing the Financial Disclosure Form (provided by Advanced Bionics in the Clinical Trial Agreement).
11. I have never participated in an investigation or other research activity which was terminated (disqualified) by FDA, the IRB (or equivalent), or sponsor of a study due to a non-compliance issue (21 CFR 812.43).
12. I further certify that I have not been debarred from FDA to participate in clinical trials. In the event that I become debarred or receive notice of action or threat of an action with respect to my debarment during the term of this Agreement, I agree to immediately notify the sponsor and the authorized IRB for my study site (21 CFR 812.119).

Signature of Investigator: _____

Date: _____

Printed Name of Investigator: _____

2.0 Protocol Synopsis

Study Title	Benefits of the HiResolution Bionic Ear System in Adults with Asymmetrical Hearing Loss
Sponsor	Advanced Bionics, LLC
Device	HiResolution Bionic Ear System (HiRes 90K™ Advantage implant with HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode or the HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode; Naída family external sound processor; and custom fitting software)
Primary Study Objective	To evaluate the benefits of unilateral implantation in adults who have severe to profound sensorineural hearing loss in one ear, and up to moderate sensorineural hearing loss in the other ear (asymmetric hearing loss).
Study Design	Prospective within-subjects repeated-measures design, each subject serves as his/her own control
Study Population	Up to 15 newly implanted adults; up to 2 participating study sites
Efficacy Objective	Efficacy data to support product approval is not part of this study. The purpose of this study is to gain insight regarding cochlear implantation in an asymmetric hearing loss clinical population. As part of this study, some audiometric, speech performance and subjective outcome data will be collected.
Safety Objective	Safety data to support product approval is not part of this study. As part of this study, adverse events will be tracked and reported to ensure that the safety of patients is maintained.
Inclusion Criteria	<u>General Requirements:</u> • Ability to provide Informed Consent • 18 years of age or older • English language proficiency • Willingness to participate in all scheduled procedures outlined in the study investigational plan • Willingness to use an approved cochlear implant signal processing strategy in an everyday listening program during study <u>*Ear to be Implanted*</u>: • Severe-to-profound sensorineural hearing loss (<u>≥</u> 70 dB HL) as defined by the pure tone average for 500, 1000, 2000 and 4000 Hz • CNC word recognition score ≤30% (tested in subject's everyday listening condition for that ear) • Duration of severe-to-profound sensorineural hearing loss (<u>≥</u> 70 dB HL) >3 months and ≤10 years in the *ear to be implanted* only <u>*Contralateral (non-implanted) ear*</u>: • Up to a moderate sensorineural hearing loss (<70 dB HL) as defined by the

	pure tone average for 500, 1000, 2000 and 4000 Hz • CNC word recognition score >30% (tested in subject's everyday listening condition for that ear)
Exclusion Criteria	• Previous experience with a cochlear implant • Cochlear malformation or obstruction (i.e. ossification) that would preclude full insertion of electrode array in the *ear to be implanted* • Medical or psychological conditions that contraindicate surgery or impact the ability to manage an implanted device or the study related procedures as determined by the investigator • Diagnosis of auditory neuropathy/dys-synchrony in either the ear to be implanted or the contralateral ear • Active middle-ear disease/infection in the *ear to be implanted* • Unrealistic expectations regarding potential benefits, risks and limitations inherent to implant surgical procedures as determined by the investigator • Unwillingness or inability of subject to comply with all investigational requirements as determined by the investigator
Efficacy Endpoints	*Implanted Ear Only:* • CNC word scores at 12 months post implantation compared to preimplant word scores *Contralateral (Non-Implanted Ear) Only:* • Unaided audiometric thresholds at 12 months post implantation test interval compared to preimplant *Bilateral Listening Condition*[‡] *(*Both Ears – Everyday Listening Condition for each ear): • AzBio sentence scores in noise at 12 months postimplantation compared to preimplant bilateral sentence scores • Lateralization ability at 12 months postoperative intervals compared to preimplantation *Quality of life/Subjective Hearing Benefit:* • Speech, Spatial, and Qualities of Hearing (SSQ) scale at 12 months compared to preimplant SSQ score • Secondary quality of life/subjective benefit endpoints include the Glasgow Benefit Inventory; Tinnitus Handicap Inventory and Sponsor developed patient report scales at 12 months postimplantation compared to preimplantation [‡]*Refer to Glossary for Definitions of Bilateral Listening Condition and Everyday Listening Condition used within this investigational plan.*
Safety Endpoints	Adverse events (AEs) will be tracked and reported according to the requirements of an IDE investigation until the study is closed. The number and percent of all subjects experiencing adverse events will be summarized by type and frequency of event. The AEs will be recorded and tracked between completion of the informed consent form (signed and dated) and two weeks after the participant's last study visit.

Study Schedule	• Consent: Subject will sign Informed Consent document prior to conduct of any study procedures
	
	• Baseline:
	  • Unaided audiometric hearing thresholds in each ear
	
	  • CNC word recognition (quiet) in each ear (tested in subject's *everyday listening condition* for that ear)
	
	  • AzBio sentence scores in noise -*bilateral listening condition*-both ears (tested in subject's everyday listening condition for each ear):
	  • Speech and Noise at 0° azimuth
	  • Speech 0° azimuth and Noise directed to side of the *non-implanted ear* (90° or 270°) and
	  • Speech 0° degree azimuth and Noise directed to the *ear to be implanted side* (90° or 270°)
	
	  • Lateralization testing using AzBio sentences in quiet - *bilateral listening condition* – both ears (tested in subject's everyday listening condition for that ear)
	
	  • Quality of Life/Subjective Hearing Benefit Questionnaires: Speech, Spatial, and Qualities of Hearing (SSQ); Tinnitus Handicap Inventory; Sponsor developed patient report questionnaire/scale(s)
	
	• Implant Surgery
	
	• Initial Device fitting and activation postimplantation;
	Unaided audiometric hearing thresholds each ear
	
	• 3 and 6 month postimplant device fitting (visits to occur within 12 and 24 weeks respectively from the initial fitting date (+/-14 days):
	
	  • CNC word scores in quiet (*implanted ear only)*
	
	  • AzBio sentence scores in noise -*bilateral listening condition*- both ears (tested in subject's everyday listening condition for each ear):
	  • Speech and Noise at 0° azimuth
	  • Speech 0° azimuth and Noise directed to side of the *non-implanted ear* (90° or 270°) and
	  • Speech 0° degree azimuth and Noise directed to the *implanted ear* (90° or 270°)
	
	  • Lateralization testing using AzBio sentences in quiet -*bilateral*

	listening condition – both ears (tested in subject's everyday listening condition for each ear) • Adjustment/optimization of program parameters as recommended by managing clinician • Quality of Life/Subjective Hearing Benefit Questionnaires: Speech, Spatial, and Qualities of Hearing Scale (SSQ); Glasgow Benefit Inventory; Tinnitus Handicap Inventory; Sponsor developed patient report scale(s) • <u>12 month postimplant device fitting (visit to occur within 48 weeks from the initial fitting date (+/-14 days):</u> • Unaided audiometric testing, each ear • CNC word scores in quiet (*implanted ear only)* • AzBio sentence scores in noise -*bilateral listening condition*- both ears (tested in subject's everyday listening condition for each ear): • Speech and Noise at 0° azimuth • Speech 0° azimuth and Noise directed to side of the *non-implanted ear* (90° or 270°) and • Speech 0° degree azimuth and Noise directed to the *implanted ear* (90° or 270°) • Lateralization testing using AzBio sentences in quiet - *bilateral listening condition* – both ears (tested in subject's everyday listening condition for each ear) • Adjustment/optimization of program parameters as recommended by managing clinician • Quality of Life/Subjective Hearing Benefit Questionnaires: Speech, Spatial, and Qualities of Hearing Scale (SSQ); Glasgow Benefit Inventory; Tinnitus Handicap Inventory; Sponsor developed patient report questionnaire/scale(s)
Efficacy Evaluations	The collection of efficacy data to support product approval is not part of this feasibility study. Pre-to postoperative comparisons of: audiometric, speech perception performance and subjective measure of perceived benefit using patient questionnaire(s) will be conducted.
Safety Evaluations	The collection of safety data to support product approval is not part of this feasibility study. Adverse events (AEs) will be tracked and reported according to the requirements of an IDE investigation until study completion.

Study Monitoring	Advanced Bionics, LLC 28515 Westinghouse Place Valencia, CA 91355 [redacted]
Data Consulting	Stat-Tech Services, LLC 501 Eastowne Drive, Suite 230 Chapel Hill, NC 27514 [redacted]

3.0 Glossary

HiResolution™ Bionic Ear cochlear implant system	An implantable medical device system designed to provide individuals who have severe-to-profound hearing loss with access to sound and improved perception of speech via electrical stimulation of the hearing nerve. It consists of (1) an externally worn sound processor (2) internal implant device with receiver stimulator electronics package and electrode array, and (3) a custom fitting software used to program the external sound processor.
HiRes family of implants	HiRes 90K™ Advantage implant with the HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode, and HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode
Sound Processor (SP)	The external part of a cochlear implant system that captures sound and converts it to digital information
Advanced Bionics SoundWave™ Professional Suite and the Clinicians Programming Interface (CPI)	Advanced Bionics commercially available fitting software platform and interface for cochlear implant sound processor fitting and programming
Everyday Listening Condition	This is used within this investigational plan to refer to a participant's typical listening condition for each ear (e.g. aided or unaided). Thus, dependent on the hearing levels in the better hearing ear, conventional amplification may or may not be utilized. Likewise, dependent on the severity of hearing loss in the poorer hearing ear, conventional amplification options such as a hearing aid, CROS, BICROS or osseointegrated system may or may not be the everyday listening condition preoperatively for the participant. Postoperatively, the poorer hearing ear is anticipated to be aided with a cochlear implant.
Bilateral Listening Condition	For purposes of this study, bilateral listening test condition refers to a participant's everyday listening condition with both ears

4.0 Purpose of the Investigation

Binaural hearing should be the standard of care for people with hearing loss. Not unlike non-auditory sensory systems (e.g. the visual system) to which treatment is approached in a bilateral approach, the hearing system is inherently constructed to receive two inputs (Ryugo and Limb, 2009). In a symmetrical hearing loss condition, despite the auditory system having reduced input, a balance exists between the two ears. Thus, when amplification options are applied depending on the degree of hearing loss (i.e. hearing aid, cochlear implant or combination) that balance and binaural processes (i.e. sound localization, spatial awareness, hearing in noise) may

be maintained. In an asymmetrical hearing loss circumstance, this binaural balance is considerably disrupted and binaural processing abilities are further compromised.

Extensive clinical evidence (i.e. results from bimodal recipients, bilateral cochlear implant recipients) supports the substantial advantages of binaural stimulation of the auditory system, including improved localization and speech understanding, particularly in the presence of background noise (Dowell et al., 2004; Lorens et al., 2008; Gstoettner et al., 2006;2008; Lenarz et al., 2009; Skarzynski et al., 2007a,b, 2010a; Adunka et al., 2008, 2010; James et al., 2006; Simpson et al., 2009; Kiefer et al., 2005; Helbig et al., 2008, 2011a,b; Gantz et al., 2005; Incerti et al., 2013; Fraysse et al., 1998; Turner et al., 2008b; Gifford et al., 2013; von Ilberg et al., 2011; Dorman et al., 2009; Novak et al., 2007; Litovsky et al., 2006, 2009, 2012; Nopp et al., 2004; Koch et al., 2009; Byrne et al., 1992; Köbler et al., 2001, 2002 ; Grantham et al., 2008).

The current treatment modality for individuals with congenital or acquired severe-to-profound sensorineural hearing loss in both ears and poor speech recognition in the best-aided condition is cochlear implantation. Standardly, health professionals recommend cochlear implantation in at least one ear under these guidelines when benefit from conventional amplification (i.e. hearing aid) is not sufficient.

Since the original approval of the multi-channel cochlear implant (1985), advances in technology, electrode design, speech coding strategies and surgical techniques have occurred at a relatively rapid rate which have led, and continue to lead to significant improvements in cochlear implant recipient performance. Just as changes to technology and technique have ensued, so has that of the profile of the cochlear implant candidate.

More recently, this standard of care treatment option has been suggested and explored for a patient population not previously considered implant candidates as a means to restore binaural hearing input. The patient population is that of single sided deafness or asymmetrical hearing loss who present with unilateral severe-to-profound hearing loss and much better hearing in the opposite ear. The underlying supposition is that such patients are able to function effectively with the better hearing ear alone even if that ear requires some amplification. However, patients with single-sided deafness or asymmetrical hearing experience considerable communicative difficulties in everyday listening environments and quality of life. This is well supported in peer-reviewed literature and research (Wie et al. 2010; Noble et al. 2008).

Historically, patient populations with substantial asymmetrical hearing loss have been underestimated as to the level of handicap this type of loss actually poses. Patients with single-sided deafness function with unilateral hearing input which can affect speech understanding, conversing in noisy environments, sound localization, (Arndt et al., 2011), directionality and spatial awareness due to the monaural acoustic stimulation. Unilateral hearing additionally demands higher concentration for listening, leading to rapid fatigue, potential misunderstandings, frustration and distractibility (Wie et al., 2010).

Treatment options for asymmetrical hearing loss have included conventional hearing aid systems (i.e. CROS or BICROS – contralateral routing of signal) or an osseointegrated/bone – anchored system (i.e. BAHA™; Ponto). While these options offer a solution, there are substantial limitations. Specifically, the current conventional options capture and route sound

received at the poorer ear and deliver at audible sensation levels to the better hearing ear and/or functioning cochlea (Roland et al., 2011; Mueller et al., 1990; Niparko et al., 2003; Lin et al., 2006) either via bone conduction or contralateral routing of the signal. However, these types of devices do not provide and/or restore *binaural* auditory input. This precludes any benefit of binaural hearing system and respective binaural auditory processes (i.e. sound localization, spatial awareness and/or improved speech perception/understanding in noise).

Another relevant aspect related to hearing loss and an asymmetric hearing loss or single-sided deafness clinical population that has been well documented in peer-reviewed studies is that of tinnitus. Tinnitus is often concomitant, and in many cases debilitating, with severe-to-profound hearing impairment (Vermeire et al., 2009; Buechner et al., 2010; Hansen et al., 2013). Conventional treatment options such as CROS or osseointegrated systems have been reported as unsuccessful in the treatment and suppression of tinnitus. This is in part related to an inability to sufficiently deliver acoustic input to the poorer ear to aid in suppression or diminution given the level of hearing loss severity; and that the conventional (i.e. CROS or BICROS) option or direct bone conduction stimulation does not stimulate the poorer ear as everything routes to the better hearing side.

Emerging research and scientific literature available to date suggests that cochlear implant is superior to current available conventional amplification options for patients with single-sided deafness or asymmetrical hearing loss after careful preoperative audiological diagnostic screening and patient selection. This is largely based on the possibility of restoring binaural hearing sensitivity with a cochlear implant. Vermeire and Van de Heyning in 2009 published one of the first studies reporting auditory outcomes of cochlear implantation in single-sided deafness (N=20 patients). Results from this study demonstrated that asymmetrically deaf patients benefited significantly in speech understanding outcomes and secondarily tinnitus suppression. Significant benefits of tinnitus abatement have been reported by various research groups and documented in peer-reviewed literature (Amoodi et al., 2011; Van de Heyning et al., 2008; Punte et al., 2011; Miyamoto et al., 1997; Battmer et al., 1989; Vermeire et al., 2009) and represents another potential advantage of electrical stimulation over conventional devices (i.e. CROS or osseointegrated options) in the treatment of patients with asymmetrical hearing loss and/or single-sided deafness.

Current research supports these initial published results and show that cochlear implantation in this clinical population is significant in helping patients improve *binaural* hearing abilities and processes, particularly speech perception enhancement in noise, sound localization and is beneficial in the reduction a number of situations in which the unilateral hearing loss was significantly problematic without this treatment (Arndt et al., 2011a; Firszt et al., 2012a,b; Vermeire and Van de Heyning, 2009; Buechner et al., 2010; Hassepass et al., 2013; Távora-Vieira et al., 2013; Blasco and Redleaf, 2014; Tokita et al., 2014; Vlastarakos et al., 2014). Lastly and importantly, current research and clinical studies have also demonstrated that cochlear implantation has had a significant qualitative improvement and impact on the perceived benefit, device acceptance and enjoyment of life (Arndt et al., 2011; Roland et al., 2011; Stelzig et al., 2011; Dwyer et al., 2014) for patients with unilateral deafness.

Although an asymmetric hearing loss of a severe-to-profound degree in one ear with much better hearing on the opposite ear (unilateral deafness/single-sided deafness) indication is not

currently approved for cochlear implantation, there is a clear, emerging interest industry-wide in this new frontier. The Sponsor believes, as supported from current research and investigators focused on treatment options for this clinical patient population, that cochlear implantation can provide a true replacement of an independent acoustic sensor to the deafened ear potentially restoring binaural hearing sensitivity.

The ability to activate binaural processes, which are innately set up in the human auditory pathway, may be an extremely viable and beneficial option to not only improve auditory performance but also, and perhaps more importantly, quality of life for this patient population. It is believed that patients will derive more gains post cochlear implant treatment than they would with present conventional treatment options (i.e. CROS, BICROS or osseointegrated systems). This new frontier is one that the Sponsor believes deserves significant focus and attention to and is proposing a feasibility study approach to evaluate this treatment option for asymmetrical hearing loss patients. This will provide basic, valuable understanding of device functionality, patient comfort, performance, ease of use and patient satisfaction in this clinical population.

5.0 Device Description(s):

5.1.1 HiResolution™ Bionic Ear Cochlear Implant System

Participants will receive and retain the commercially available HiResolution™ Bionic Ear cochlear implant system (internal and external device) at the time of implantation.

The HiResolution™ Bionic Ear cochlear implant system consists of:

(1) an externally worn sound processor (i.e. Naída CI family sound processor)

(2) internal components consisting of an implantable electronics package and electrode (e.g. HiRes family of implants [HiRes 90K™ Advantage implant with the HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode, and HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode]) and

(3) a custom fitting software used to program the external sound processor

5.1.2 Programming Software/Listening Program(s) and Feature(s)

Participants cochlear implant system(s) will be programmed at his/her managing implant center using the commercially available Advanced Bionics programming software, SoundWave™ Professional Suite and the Clinicians Programming Interface (CPI).

6.0 Study Objectives

The proposed clinical feasibility study is to obtain evaluate the benefits of unilateral implantation in adults who have severe to profound sensorineural hearing loss in one ear, and up to moderate sensorineural hearing loss in the other ear (single-sided deafness or asymmetric

hearing loss). Objective audiometric and speech recognition outcomes, in addition to subjective outcomes with the investigational external device system and components will be obtained at scheduled study test intervals at the participating study centers.

6.1 Study Duration

The study endpoint for an enrolled participant in this feasibility study is following the participant's completion of the twelve (12) month post-device activation interval. It is expected that study participation for a participant enrolled in the feasibility study will involve a 15-19 month commitment allowing for pre- to- postoperative assessments and test intervals. The maximum duration of a study participant's enrollment in the feasibility study will be up to 19 consecutive months.

7.0 Study Protocol

7.1 Study Design and Justification

This study uses a prospective within-subjects repeated-measures design in which each subject serves as his/her own control. Single-subject repeated-measures study design is appropriate as it accommodates the heterogeneity that characterizes hearing-impaired populations. As it is not feasible to conceal the presence or absence of a cochlear implant or hearing instrument from device recipients and/or clinical investigators a blinding procedure would not be an appropriate trial design for this feasibility study. Adverse events will be tracked and reported to the FDA according to the requirements of an IDE investigation until the study is closed. The AEs will be recorded and tracked between completion of the informed consent form (signed and dated) and two weeks after the participant's last study visit.

7.2 Study Endpoints

7.2.1 Efficacy

The purpose of the proposed feasibility study is to evaluate and gain insight regarding cochlear implantation in an asymmetric hearing loss clinical population. Some speech performance and subjective outcome data will be collected during the study. Efficacy data to support product approval is not part of this study.

7.2.2 Safety

Safety data to support product approval is not part of this study. Adverse event data will be collected and evaluated during the feasibility study to ensure that the safety of patients is maintained as per requirements of an IDE and respective center Institutional Review Board guidelines for reporting.

7.3 General Subject Population

The Sponsor expects to implant up to 20 subjects in this clinical feasibility study across 12 study sites in the United States. Prior to recruitment, written approval of the investigational plan and informed consent form will be obtained from the FDA and associated participating study center Institutional Review Boards (IRB). Study participants are required to meet the study inclusion criteria (provided below) as determined by the respective, referring medical/hearing care providers. All consented participants meeting the study inclusion criteria and not meeting any of the exclusion criteria will be implanted with the commercially available HiResolution Bionic Ear Cochlear Implant System (HiRes 90K™ Advantage implant with the HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode or the HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode and currently commercially available AB sound processor (i.e. Naída family external sound processor). A participant's ability to undergo the surgical procedure for cochlear implantation is determined respectively by the participant's managing medical/hearing care providers at his/her implant center.

7.4 Inclusion and Exclusion Criteria

General Inclusion criteria:

- Ability to provide Informed Consent
- 18 years of age or older
- English language proficiency (to be confirmed via case history as having graduated 8th grade level)
- Willingness to participate in all scheduled procedures outlined in the protocol
- Willingness to use an approved cochlear implant signal processing strategy in an everyday listening program during study

Audiometric Inclusion criteria:

Ear to be Implanted:

- Severe-to-profound sensorineural hearing loss (>70 dB HL) as defined by the pure tone average for 500, 1000, 2000 and 4000 Hz
- CNC word recognition score up to ≤30% (tested in subject's everyday listening condition for that ear)
- Duration of severe-to-profound sensorineural hearing loss (>70 dB HL) >3 months and ≤10 years in the ear to be implanted only

Contralateral (non-implanted) ear:

- Up to a moderate sensorineural hearing loss (<70 dB HL) as defined by the pure tone average for 500, 1000, 2000 and 4000 Hz
- CNC word recognition score >30% (tested in subject's everyday listening condition for that ear)

Exclusion Criteria:

- Previous experience with a cochlear implant
- Cochlear malformation or obstruction (i.e. ossification) that would preclude full insertion of electrode array in the *ear to be implanted*
- Medical or psychological conditions that contraindicate surgery or impact the ability to manage an implanted device or the study related procedures as determined by the investigator
- Diagnosis of auditory neuropathy/dys-synchrony in either the ear to be implanted or the contralateral ear
- Active middle-ear disease/infection in the *ear to be implanted*
- Unrealistic expectations regarding potential benefits, risks and limitations inherent to implant surgical procedures as determined by the investigator
- Unwillingness or inability of subject to comply with all investigational requirements as determined by the investigator

7.5 Participant Withdrawal

Study participants may withdraw from the study at any time, with or without reason, and without prejudice to further treatment. The study site investigator(s) and/or study Sponsor has the right to discontinue study participants. Participants can be discontinued for the following reasons:

- Voluntary withdrawal of consent made by the participant
- A safety concern identified by the Principal Investigator, the Sponsor, or any third party
- 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

Participants who withdraw or who are discontinued from the study will be reported accordingly to the Institutional Review Board. If a subject was discontinued because of a device-related adverse event or serious adverse event (SAE), the subject must be followed until the serious adverse event is resolved, the point at which the subject withdraws HIPAA authorization, or the study is concluded.

The Investigator (or authorized delegate) in cooperation with the study monitor will complete a tracking log and/or enter into the electronic data capturing system the disposition of each enrolled subject (completed study, withdrew, discontinued).

8.0 Study Procedures

8.1 Recruitment

Participants who meet the study criteria will be recruited from adult hearing-impaired patient populations at the participating study centers. A participant's willingness and ability to meet the follow-up requirements will be determined and informed consent will be obtained. A signed and dated informed consent will be kept in the participant's study record and copy provided to the participant. Study participants must also sign a release that authorizes access of medical records to the study sponsor, investigators, monitors and the FDA prior to proceeding with screening assessments. This release may be its own signature line contained within the Informed Consent Form (see Appendix B for template) or may be a separate authorization, consistent with institutional policy.

8.2 Participant Screening

No investigational procedures are used to screen patients for study eligibility. Subjects eligible to participate in this study will be evaluated according to the inclusion requirements for the study. Informed consent will be obtained before any study-specific tests or procedures are conducted. An individual is considered to be enrolled as a study participant only after the informed consent document has been signed and dated. Each subject will be assigned a unique identifier at the time of enrollment.

8.3 Test Metrics or Procedures

The monosyllabic CNC word test will be used as the primary test metric for preimplant candidacy determination and follow-up postimplant performance assessments in the treated ear. The AzBio Sentence test in noise will be used as the primary test metric to assess the binaural hearing condition (implanted + non-implanted ear) performance pre-to-postoperatively.

Given the asymmetrical clinical population for which this feasibility study is being conducted, standard audiometric clinical masking procedures during audiometric and speech perception metrics will be applied as needed to reduce any potential contribution of the better hearing ear during these assessments.

In order to isolate the ear to be implanted and/or treated ear during certain test conditions (i.e. aided testing), a foam earplug and an over-the-head earmuff will be used in the contralateral (non-implanted ear). This method will be referred to in the remainder of this document as 'plug and muff.'

8.3.1 Audiometric Measures:

Standard audiometric practice and procedures are applied for the testing of inter-octave frequencies if necessary.

- Unaided air conduction thresholds using insert earphones at octave frequencies will be obtained for each ear at 250, 500, 1000, 2000, 4000 and 8000 Hz. Clinical masking used as appropriate.

- Unaided bone conduction hearing thresholds for each ear at 500, 1000, 2000 and 4000 Hz

8.3.2 Speech Perception Measures:

General speech perception testing procedures

All speech perception testing will be conducted using recorded stimuli presented from a single loudspeaker in at a minimum a single-walled sound booth capable of accommodating a calibrated, 90 degree speaker orientation. Audiometers will conform to ANSI standards for pure-tone and speech audiometry and/or Manufacturer Specifications.

Speech perception measures conducted in soundfield are to be administered via a loudspeaker at 0° azimuth at a distance of one meter from the subject. Speech signals will be presented at 60 dB A. Speech levels will be calibrated to 60 dB SPL using a microphone placed at the approximate position of the subject's head (one meter from loudspeaker).

Speech stimuli may be administered via an audiometer using the proprietary software developed by Advanced Bionics called ListPlayer. [redacted]

IMPORTANT NOTE REGARDING POSTOPERATIVE TESTING: ***Audiometric and speech perception testing at post device activation intervals is to be conducted prior to any device re-programming and/or adjustment of MAP parameters. It is recommended that a listening check of the participant's device and confirmation of sufficient battery life be verified prior to testing at each study interval.***

Consonant-Nucleus-Consonant (CNC) Word Recognition Test

The CNC monosyllabic word test (Peterson and Lehiste, 1962) is a validated test of open-set word recognition ability. The test will be administered in quiet at 60 dBA (target 0° azimuth) and scored as total number of words correct which will be expressed for results/reporting as percentage correct. The CNC word test is the primary speech perception metric used for study inclusion determination and postoperative outcome comparison at defined intervals for this feasibility study.

AzBio Sentence Test

The AzBio Sentence Test (Spahr and Dorman, 2005) is a validated test of open-set sentence recognition ability. The test is scored as total number of words correct which is expressed for results/reporting as percentage correct. The sentence test tokens include

both male and female speakers. The AzBio Sentence test will be administered at 60 dBA + 5 dB SNR in noise using Speech-spectrum Noise (SSN) in three conditions:

- Speech Front, Noise Front (Target and noise 0° azimuth)
- Speech Front (0° azimuth), Noise directed to the *ear to be implanted/implanted* ear (90° or 270° azimuth)
- Speech Front (0° azimuth), Noise directed to the *non-implanted* ear (90° or 270° azimuth)

Lateralization Testing

The AzBio Sentence test will additionally be used as the metric to assess lateralization. The test will be administered in soundfield in quiet at 40 dBA. The participant will be positioned face-forward and centered between the right and left speakers (located at 45°) and at a one meter distance (typical calibrated test position) in the audiometric sound suite. A single list of interleaved sentences varying between right and left speaker presentations will be administered. The participant will be asked to identify if the sentence is heard from the right or left speaker. Scoring is based on number correct that the participant identifies from which speaker the sentence was detected.

8.3.3 Patient Questionnaire(s):

Speech, Spatial and Sound Qualities Questionnaire (SSQ)

The SSQ (Gatehouse and Noble, 2004; Noble and Gatehouse 2006) will be used as a subjective, self-reported assessment of hearing status and hearing capability in everyday life prior to and during the feasibility study. The questionnaire is designed to measure self-reported auditory disability across a wide variety of domains to include: hearing speech in a variety of competing contexts; directional, distance and movement components of spatial hearing; segregation of sounds and attending to simultaneous speech streams; ease of listening; naturalness; clarity and identifiability of different speakers and music. The current standard versions of SSQ (5.6) and SSQ-B (5.6) will be used in the study.

Glasgow Benefit Inventory (GBI)

The GBI (Robinson, Gatehouse and Browning, 1996) is a subjective, postintervention questionnaire developed specifically to evaluate any otorhinolaryngological (ORL) interventions. Patient benefit is the change in health status resulting from the intervention. The GBI will be administered postoperatively.

Tinnitus Handicap Inventory (THI)

The THI (Newman, Jacobson and Spitzer, 1996) will be used as a subjective, self-reported measure to quantify the impact of tinnitus on daily living. The questionnaire will be administered pre and postoperatively only if the participant reports tinnitus.

Additional Metrics:

Sponsor developed patient-report subjective questionnaire/scales such as sound quality and/or quality of life related aspects may additionally be administered at various study intervals during the feasibility study only to obtain further relevant input from patients

with this clinical hearing profile receiving this type of treatment. The study intervals are identified within the study protocol when Sponsor developed subjective assessments are to be used.

9.0 Study Visits

Baseline Visit

Signed Informed Consent is to be obtained prior to the conduct of any study procedures. Baseline information consists of collection of participant demographics, hearing and pertinent medical history, hearing history (i.e. etiology and onset of hearing loss, date of birth, gender, duration of hearing loss, amplification use). With respect to amplification use, the licensed/certified hearing care professional will determine if a potential study participant has had an adequate and/or appropriate trial using conventional amplification available for single-sided deafness and asymmetrical hearing loss.

The following test measures are administered at the Baseline Visit:

Audiometric Testing:

- Unaided air-conduction thresholds using insert earphones at 250, 500, 1000, 2000, 4000 and 8000 Hz; unilateral, each ear. Clinical masking as appropriate.

- Unaided bone-conduction hearing thresholds at 500, 1000, 2000 and 4000 Hz; unilateral, each ear

Speech Perception Testing:

- Separate Ear CNC Word Test - Two lists of 50 words tested *in the participant's* ***everyday listening condition*** *for that ear*, thus:

    - If the test ear is unaided (participant does not utilize conventional amplification such as a hearing aid, CROS, BICROS or osseointegrated system), measurement of CNC words using insert earphones presented at 60 dBA will be conducted.

    - If the test ear is aided with conventional amplification (i.e. hearing aid, CROS, BICROS or osseointegrated system), measurement of CNC words is conducted in soundfield at 60 dBA (Target 0° Azimuth) with the plug and muff method in use for the non-test ear (better hearing ear) to eliminate from potential cross-over and/or contribution to the outcome.

- AzBio Sentence Test in Noise - Two lists presented in the following soundfield conditions at 60 dBA with a +5 dB SNR using speech-spectrum noise *in the participant's bilateral, everyday listening condition*. Note: Participants may or may not be aided in one or both ears thus, testing may be aided or unaided or a combination during AzBio Sentence test administration). The following test conditions will be conducted:

- Speech Front, Noise Front (Target and Noise 0° azimuth)

- Speech Front (0° azimuth), Noise directed to the *ear to be implanted* (90° or 270° azimuth)

- Speech Front (0° azimuth), Noise directed to the *contralateral/non-implanted* ear (90° or 270° azimuth)

Lateralization Testing:

- Using AzBio Sentence Test in Quiet - One list presented at 40 dBA in soundfield in *the participant's bilateral, everyday listening condition*. The participant is asked to identify if the sentence was detected from the left or right speaker. The sentence delivery from right or left speaker is randomized.

  Note: Participants may or may not be aided in one or both ears thus, testing may be aided or unaided or a combination during test administration). The test setup is as follows:
  - Participant will be centered and faced forward between a right and left speaker (each positioned in corners of the audiometric suite at 45° respectively)

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ) Questionnaire standard version (Version 5.6)
- Tinnitus Handicap Inventory (THI) – ***Administered only if participant has reported tinnitus***
- Sponsor developed patient report questionnaire/scale

Implant Surgery:

Conducted at participant's managing hearing care clinical center. *Note: Implant surgery to be completed within 26 weeks of the Baseline Visit. If the surgery date exceeds this time frame, Baseline measures including audiometric and speech perception testing will need to be re-evaluated.*

Initial Device Activation/Fitting:

Device activation should occur within 3 to 6 weeks postimplant surgery.

Device Programming – Sound Processor Fitting:
Specific Instruction:

- Study participants are to be provided with a standard everyday program with the following FDA approved signal processing strategy(ies):
  HiRes™ Optima with *ClearVoice*

Additional programs and parameter settings are deferred to the guidance and recommendations of the participant's managing hearing care specialist.

Audiometric Testing:

- Unaided air-conduction thresholds using insert earphones at 250, 500, 1000, 2000, 4000 and 8000 Hz; unilateral, each ear. Clinical masking as appropriate.

- Unaided bone-conduction hearing thresholds at 500, 1000, 2000 and 4000 Hz; unilateral, each ear

Adverse Event Assessment:

An adverse event assessment is completed by the investigator at each test interval. An assessment will be completed additionally if an adverse event has occurred outside of the scheduled study test intervals (i.e. unscheduled visit).

3 and 6 Month Postimplant Test Intervals:

The three and six month post-device activation visits to occur within 12 and 24 weeks respectively (+/- 14 days) of the participant's device activation date.

Important Note: The participant is to be tested at each scheduled study test interval using the standard everyday program (HiRes™ Optima program with ClearVoice). Please confirm that this program is selected prior to testing.

Speech Perception Testing:

- CNC Word Test in Quiet - Two lists of 50 words presented at 60 dBA in the *implanted ear only* (plug and muff method to be used in the contralateral/non-implanted ear during testing)

- AzBio Sentence Test in Noise - Two lists presented in the following soundfield conditions at 60 dBA with a +5 dB SNR using speech-spectrum noise *in the participant's everyday, bilateral listening condition*. The following test conditions will be conducted:

    - Speech Front, Noise Front (Target and Noise 0° azimuth)

    - Speech Front (0° azimuth), Noise directed to the *implanted ear* (90° or 270° azimuth)

    - Speech Front (0° azimuth), Noise directed to the *non-implanted* ear (90° or 270° azimuth)

Lateralization Testing:

- AzBio Sentence Test in Quiet - One list presented at 40 dBA in soundfield *in the participant's everyday bilateral listening condition*. The participant is asked to identify if the sentence was detected from the left or right speaker. The sentence delivery from right or left speaker is randomized.

Note: Participants may or may not be aided in one or both ears thus, testing may be aided or unaided or a combination during test administration). The test setup is as follows:

- Participant will be centered and faced forward between a right and left speaker (each positioned in corners of the audiometric suite at 45° respectively)

Self-Assessment Questionnaire(s):

- The Speech, Spatial and Sound Qualities Questionnaire SSQ-B (Version 5.6) is to be administered at the 3 and 6 month test intervals
- Tinnitus Handicap Inventory (THI) – ***Administered only if participant has reported tinnitus***
- Glasgow Benefit Inventory
- Sponsor developed patient report questionnaires/scales

Adverse Event Assessment:

An adverse event assessment is completed by the investigator at each test interval. An assessment will be completed additionally if an adverse event has occurred outside of the scheduled study test intervals (i.e. unscheduled visit).

Device Re-Programming (if necessary)

- Adjustment/optimization of participant's device program as recommended by managing clinician.

12 Month Postimplant Test Interval:

The twelve month post-device activation visit to occur within 48 weeks (+/-14 days) of the participant's device activation date.

Important Note: The participant is to be tested at each scheduled study test interval using the standard everyday program ([redacted]). Please confirm that this program is selected prior to testing.

Audiometric Testing:

- Unaided air-conduction thresholds using insert earphones at 250, 500, 1000, 2000, 4000 and 8000 Hz; unilateral each ear. Clinical masking as appropriate.

- Unaided bone-conduction hearing thresholds at 500, 1000, 2000, and 4000 Hz; each ear.

Speech Perception Testing:

- CNC Word Test in Quiet - Two lists of 50 words presented at 60 dBA in the *implanted ear only*

- AzBio Sentence Test in Noise - Two lists presented in the following soundfield conditions at 60 dBA with a +5 dB SNR using speech-spectrum noise *in the participant's everyday, bilateral listening condition*. The following test conditions are to be conducted:

    - Speech Front, Noise Front (Target and Noise 0° azimuth)

    - Speech Front (0° azimuth), Noise directed to the *implanted ear* (90° or 270° azimuth)

    - Speech Front (0° azimuth), Noise directed to the *non-implanted* ear (90° or 270° azimuth)

Lateralization Testing:

- AzBio Sentence Test in Quiet - One list presented at 40 dBA in soundfield in *the participant's bilateral, everyday listening condition*. The participant is asked to identify if the sentence was detected from the left or right speaker. The sentence delivery from right or left speaker is randomized.

  Note: Participants may or may not be aided in one or both ears thus, testing may be aided or unaided or a combination during test administration. The test setup is as follows:
    - Participant will be centered and faced forward between a right and left speaker (each positioned in corners of the audiometric suite at 45° respectively)

Self-Assessment Questionnaire(s):

- Important Note: The Speech, Spatial and Sound Qualities Questionnaire standard SSQ version (5.6) is administered at this test interval.
- The Tinnitus Handicap Inventory (THI) – ***Administered only if participant has reported tinnitus***
- Glasgow Benefit Inventory
- Sponsor developed patient report questionnaire/scale

Adverse Event Assessment:

An adverse event assessment is completed by the investigator at each test interval. An assessment will be completed additionally if an adverse event has occurred outside of the scheduled study test intervals (i.e. unscheduled visit).

Device Re-Programming (if necessary)

- Adjustment/optimization of participant's device program as recommended by managing clinician.

9.1 Summary of Data Collection at Study Test Intervals:

Test Measure/ Activity	Condition	Preoperative	Postoperative Intervals			
		Baseline	Initial Device Activation	3 Month	6 Month	12 Month
Informed Consent		X				
Demographics and Hearing History		X				
Objective Measures						
Unaided Audiometric Testing (Air/Bone Conduction)	Unilateral, each ear	X	X			X
CNC Words – Quiet 60 dBA	Unilateral, each ear	X				
	Treated Ear			X	X	X
AzBio Sentences – Noise (60 dBA + 5 dB SNR)	Bilateral Listening Condition/ Everyday Listening Condition	X		X	X	X
Lateralization Task using AzBio Sentences in Quiet – 40 dBA	Bilateral Listening Condition/ Everyday Listening Condition	X		X	X	X
Subjective Measures						
SSQ		X		X	X	X
GBI				X	X	X
THI[1]		X		X	X	X
Sponsor developed patient report questionnaire/scale		X		X	X	X

[1]*Participants that do not report tinnitus pre or postoperatively are not administered the THI questionnaire.*

10.0 Statistical Methods

General Considerations: Statistical Methods and Sample Size

Individual outcomes will be compared across pre- and postoperative test conditions for audiometric and speech performance outcomes. No formal statistical hypothesis will be tested. At a minimum, individual data/outcomes will be tabulated and summarized for audiometric and speech performance outcomes to establish numbers of subjects showing improvement, no change or decrease in performance. Descriptive statistics may consist of counts, means, median and standard deviations, percent and relative frequency for categorical variables (i.e.

questionnaire). The proposed sample size the Sponsor is aiming to recruit for participation of up to 15 total subjects is deemed sufficient for this feasibility study.

11.0 Efficacy Measures

Collection of efficacy data to support product approval is not part of this feasibility study. As such, no formal statistical hypothesis is being posed and/or applied. As part of this feasibility study, the following data will be collected and evaluated:

1. Monosyllabic word recognition performance in quiet using the CNC word test pre-to post device activation at 12 months will be compared, tabulated and summarized. Specifically, the CNC word scores postoperatively will be compared to the pre-implant word score for the implanted ear. Individual and group comparisons will be completed. The intent is to understand the benefit of the implant treatment option and restoration of auditory input results in improved speech understanding.

2. Audiometric hearing thresholds at the 12 month postoperative test interval will be compared to preimplant thresholds. Individual and group comparison is confirmatory to assess that hearing acuity in the non-implanted ear (better hearing ear) is not affected significantly by cochlear implant treatment in the opposite ear (poorer hearing ear).

3. Sentence recognition scores in noise using the AzBio Sentence Test pre-to-post device activation will be compared, tabulated and summarized. Specifically, the everyday, bilateral listening condition AzBio sentence scores at the 12 month postimplant test interval will be compared to the preimplant bilateral sentence score. Individual and group comparisons will be conducted. The intent of this comparison is to evaluate the contribution and/or benefit of the implant treatment option (provision of binaural sensory input) in an asymmetrical hearing loss population.

4. To understand if the restoration of binaural sensory input in a single-sided deafness/asymmetrical hearing loss population results in improved ability in lateralization of sound. Using the AzBio Sentence metric, the month postimplant outcome will be compared to preoperative ability. Individual and group comparisons will be conducted.

5. The Speech, Spatial Qualities (SSQ) questionnaire score comparison pre-to-post device activation will be conducted to provide a subjective measure of patient perceived hearing performance/auditory benefit with this combined technology. The SSQ will aid in providing a measure of subjective perceived benefit in the restoration of binaural auditory input. SSQ scores at 12 months postimplant will be compared to the preimplant scores. Individual and group comparisons will be conducted.

6. Additional subjective outcome scales may also be assessed and evaluated to understand if restoration of binaural auditory input results in improvement of quality of life. This will include the Tinnitus Handicap Inventory and Sponsor developed subjective scales.

The results of the efficacy measures are expected to be generalizable to the Medicare beneficiary population. It has been shown that elderly patients can benefit from cochlear

implantation and age is not considered a limitation for cochlear implant surgery (Otol Neurotol. 2016 Jan;37(1):46-51. Outcomes After Cochlear Implantation in the Very Elderly. Wong DJ1, Moran M, O'Leary SJ.). The findings of several studies suggest that cochlear implantation can be equally effective in improving speech recognition in older patients as compared to younger adults (Schwab, B., Gandolfi, M., Lai, E., Reilly, E., Singer, L. and Kim, A.H. (2015) The Impact of Age on Cochlear Implant Performance. International Journal of Otolaryngology and Head & Neck Surgery, 4, 329-337., Zwolan, T.A., Henion, K., Segel, P., Runge, C. (2014). The role of age on cochlear implant performance, use, and health utility: a multicenter clinical trial. Otol Neurotol. 35(9):1560-8; Otol Neurotol. 2017 Jan;38(1):54-59. Cochlear Implantation in the Elderly: Does Age Matter? Rohloff K1, Koopmann M, Wei D, Rudack C, Savvas E.; Rev Laryngol Otol Rhinol (Bord). 2013;134(3):119-24. Cochlear implantation in older patients: outcomes and comparisons. Rafferty A, Tapper L, Strachan D, Raine C.)

Efficacy results will be published on clinicaltrials.gov within one (1) year of the completion date of the study.

12.0 Safety Measures

The collection of safety data to support product approval is not part of this study. For these objectives, safety is referred to as freedom from procedure and/or device-related adverse events. No formal statistical hypothesis will be sought.

Safety results will be published on clinicaltrials.gov within one (1) year of the completion date of the study.

12.1 Adverse Event Reporting and Assessment

An adverse event (AE) is defined as any undesirable clinical occurrence experienced by a study subject when using the HiResolution System or when undergoing research procedures, whether or not the AE is considered to be device-related. The definition of an AE also includes any event related to any study procedures or to any underlying medical condition present at baseline that increases in severity during the study. An underlying medical condition that was present at the time of enrollment will not be reported as an AE, but any increase in severity during the study will be reported as an AE.

All device-related and non-device-related adverse events (AEs) will be tracked and reported accordingly throughout the feasibility study as defined above in the investigational plan and in accordance with requirements of an IDE investigation. The AEs will be recorded and tracked between completion of the informed consent form (signed and dated) and two weeks after the participant's last study visit. The number and percent of all subjects experiencing adverse events will be summarized by type and frequency of event. Adverse Events will be recorded and will include but are not limited to the following information [refer to Appendix A for Case Report Forms (CRFs)]:

The following risks associated with surgery and/or cochlear implantation are identified as *anticipated* Adverse Events:

- General risks
  - General anesthesia
  - Postoperative pain
  - Bleeding or infection
  - Possibility of damage to the facial nerve
  - Balance related issues (i.e. dizziness, vertigo)
  - Numbness
  - Swelling or discomfort around the ear
  - Taste disturbance
  - Increased ringing in the ears (tinnitus)
  - Neck pain
  - Skin reaction
  - Leakage of inner ear fluid or cerebrospinal fluid which may increase the risk of meningitis. Meningitis is an infection in the fluid and tissue that surround the brain and spinal cord. There are two types viral and bacterial meningitis; bacterial being the most serious type and has been reported in cochlear implant recipients. The Centers for Disease Control (CDC) recommends for patients pursuing cochlear implantation to be up to date on age-appropriate pneumococcal vaccination. More information about the CDC recommendations can be found at http://www.cdc.gov or by calling 1-800-232-2522. It is recommended to discuss vaccinations and surgical risks with the subjects prior to the scheduled procedure.
  - Hearing may sound different when the cochlear implant is turned on
  - Insertion of a cochlear implant electrode will likely result in the loss of any residual hearing in the implanted ear.

- Risks associated with implantation of the internal cochlear implant device and electrode array
  - The presence of a foreign body (implant) may result in irritation
  - Redness or breakdown of the skin in the area around the implant receiver/stimulator and/or rejection of the device
  - The electrode array may migrate partially resulting in reduced hearing ability
  - Misplacement of the electrode array may result in non-auditory sensations which may require additional medical treatment, surgery and/or removal of the device, however, this is considered a rare circumstance
  - Electrical stimulation may increase tinnitus, facial nerve stimulation, balance related issues (i.e. dizziness, vertigo) or pain
  - Implantation in the cochlear may preclude the use of future implant technology

- Device failure of operation that may perhaps require removal of the device
- A risk of additional loss natural hearing as a factor of chronological age (i.e. presbycusis) and/or etiology of the hearing loss may be experienced
- Any study participant experiencing a shift in audiometric threshold of 30 dB or greater pure tone average threshold shift across 250-1000 Hz from baseline to post-operative visits will be reported as an anticipated Adverse Event under this feasibility study.

- Risks specifically associated with the clinical population evaluated in this feasibility study, that of single-sided deafness/asymmetrical hearing loss
  - It is possible that the electrical stimulation of the cochlear implant when provided to a poorer hearing ear that has not heard for some period of time may take a period of adjustment and may subjectively be a competing signal and potentially create binaural interference. Speech perception ability in noise and sound localization ability may be impacted. Should this binaural interference occur to a level in which speech understanding is affected, the participant will have the option to remove the external cochlear implant sound processor. This removal may be dependent on the listening environment or in specific listening conditions. If the latter event occurs, and the participant chooses removal of the cochlear implant sound processor, he/she will be counseled by the managing hearing care specialist as to the alternative, conventional options and/or a return to an untreated state. These risks and mitigations are further provided below in Section 13.1 of the Investigational Plan.

The following definitions will be used to classify AEs.

A *serious adverse event* (SAE) is an event that: a) led to a death, or b) led to a serious deterioration in the health of the subject that:

- resulted in a life-threatening illness or injury,
- resulted in a permanent impairment of a body structure or of a body function,
- required inpatient hospitalization or prolongation of existing hospitalization,
- resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function, or
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

An adverse device effect (ADE) is any untoward and unintended response to a medical device. A *serious adverse device effect* (SADE) is an event related to the device 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, will be recorded on the Adverse Event Report Case Report Form [CRF] (see Appendix A for all CRFs). Information to be recorded on the CRF should include, but is not limited to:

- Date of onset of the adverse event
- Date reported to the Sponsor
- Description of the event, duration and severity
- Seriousness
- Treatment/Intervention – course of action taken
- Outcome/Status (resolved, improving, no change, worsening). In case of an SAE, the subject must be followed until the serious adverse device effect is resolved or no reasonable improvement is expected.

Evaluation of any SAE, SADE, or UADE will be conducted promptly. All AEs related to the HiResolution system that impact device safety in the first three months after device implantation will be adjudicated by a Medical Monitor. Confirmed UADEs will be reported to the FDA according to 21 CFR Part 812.150(b) (1) within 10 days after receiving [redacted]e of the event, to participating Investigators and to IRBs according to their requirements. 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 no later than 5 working days after the determination is made and no later than 15 working days after Advanced Bionics/Clinical Research first received notice of the event.

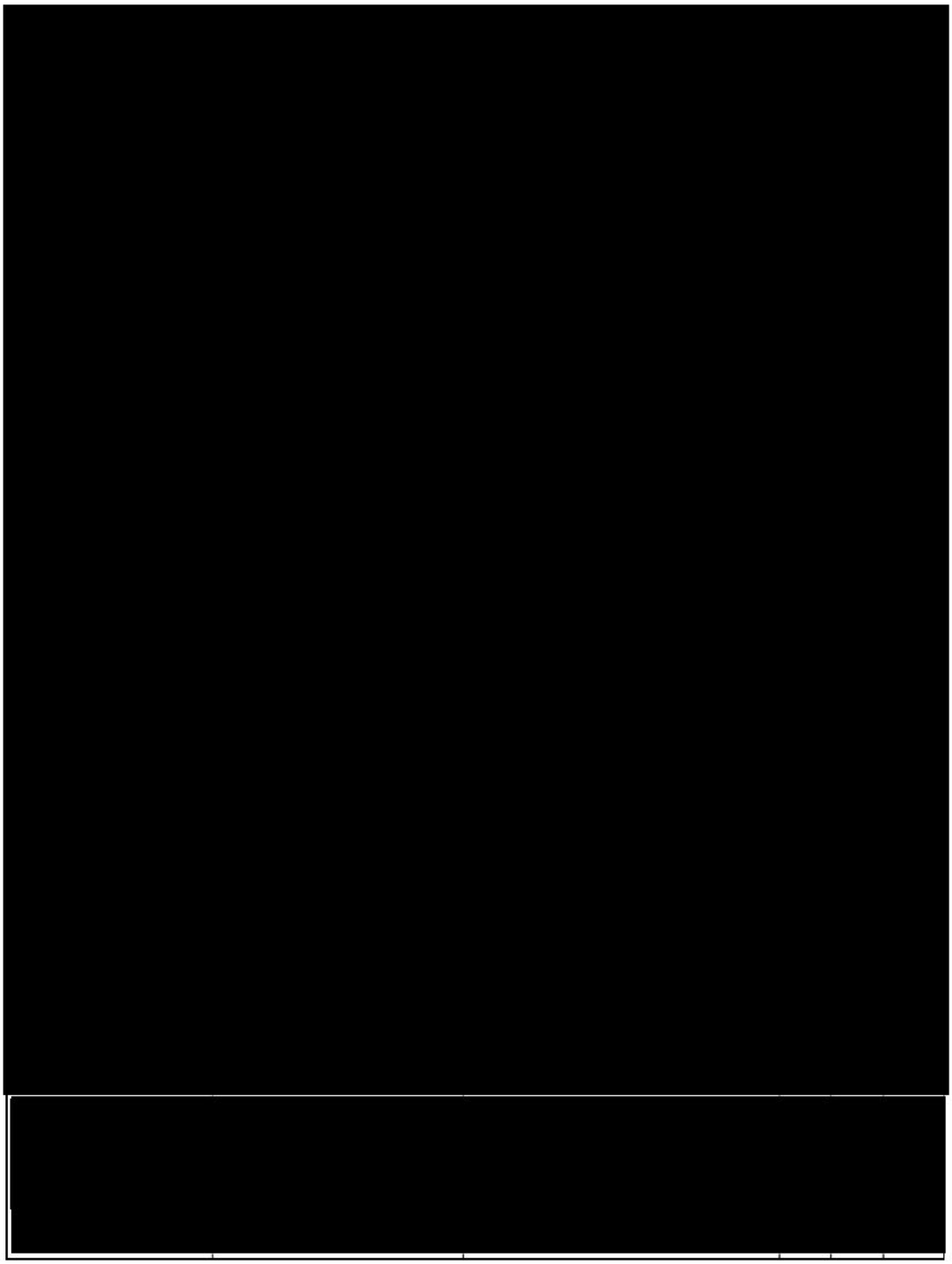
13.0 Risk Analysis

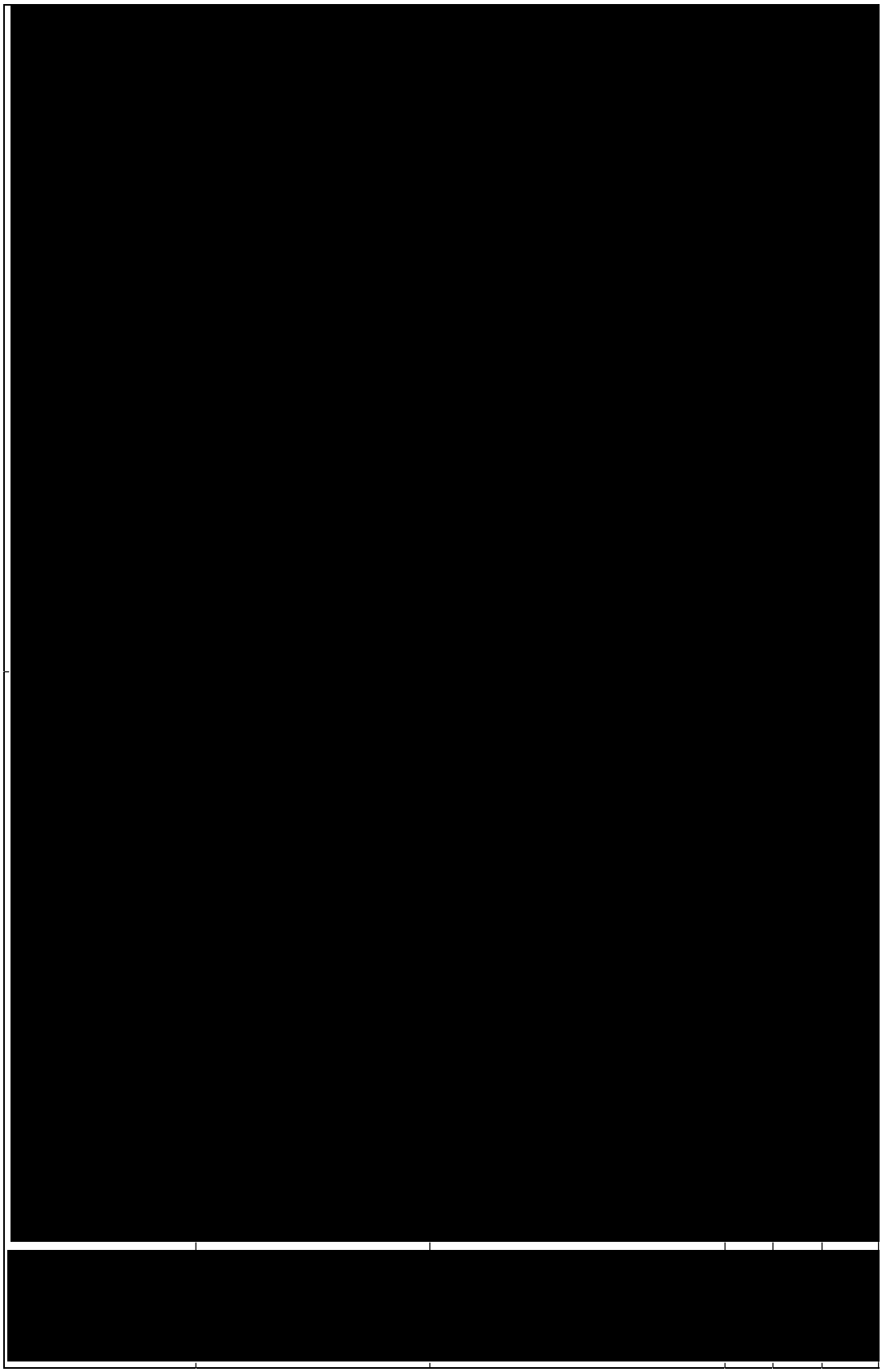
13.1 Approved products:

The HiResolution Bionic Ear System with the HiRes 90K™ Advantage implant with the HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode or the HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode and external processors (i.e. Naída family) are approved under P960058. The commercially approved and available custom fitting software, SoundWave™ Professional Suite, and Clinician's Programming Interface (CPI) will be used during this study to program the Advanced Bionics HiResolution Bionic Ear System, external cochlear implant sound processor. No investigational software will be used during this study. The risks associated with use of the approved products are contained in those products' instructions for use.

13.1 Risks related to Investigational Use Case:

Risk associated with this new investigational use-case are covered in the Risk Analysis Report for HR90K system in Single Sided Deafness (SSD) Application – D000013514 (Attachment 1.0). The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk.





[redacted]

13.2 Safety Testing of Investigational Software

Investigational software is not applicable for this feasibility study.

13.3 Surgical Risks

Risks associated with the surgical procedure of the commercially available HiResolution Bionic Ear System (HiRes 90K™ Advantage implant with the HiFocus™ 1J electrode, HiRes 90K™ Advantage implant with the HiFocus Helix™ electrode, HiRes 90K™ Advantage implant with the HiFocus™ Mid-Scala electrode or the HiRes™ Ultra Implant with the HiFocus™ Mid-Scala electrode are no greater than those associated with cochlear implantation in general and do not add any additional risks to the surgery or the post-operative healing process beyond that of other commercially approved cochlear implants. [redacted]

The study population (single-sided deafness/asymmetric hearing loss) for this feasibility study is adults who have severe to profound sensorineural hearing loss in one ear (severe-to-profound hearing loss), and up to moderate sensorineural hearing loss for the other ear.

Cochlear implantation in individuals in this population offers the provision of binaural sound input. The improvement of binaural auditory input, hence activation of binaural processes in this clinical study population is anticipated to have a significant benefit including qualitative improvement in speech understanding and importantly quality of life. Therefore, the risk/benefit ratio is expected to be low and acceptable.

Risks associated with all cochlear implant surgeries include: general anesthesia risks; postoperative pain, bleeding or infection; possibility of damage to the facial nerve; balance related issues (i.e. dizziness; vertigo); numbness, swelling or discomfort around the ear; taste disturbance, increased ringing in the ears (tinnitus); neck pain, skin reaction; leakage of inner ear fluid or cerebrospinal fluid which may increase a risk of meningitis. Meningitis is an infection in the fluid and tissue that surround the brain and spinal cord. There are two types viral and bacterial meningitis; bacterial being the most serious type and has been reported in cochlear implant recipients. The Centers for Disease Control (CDC) recommends for patients pursuing cochlear implantation to be up to date on age-appropriate pneumococcal vaccination prior to

the surgery date. More information about the CDC recommendations can be found at http://www.cdc.gov or by calling 1-800-232-2522.

The presence of a foreign body (the implant) may result in irritation, redness or breakdown of the skin in the area around the implant receiver/stimulator and/or rejection of the device; the electrode array may migrate partially resulting in reduced hearing ability; misplacement of the electrode array may result in non-auditory sensations which may require additional medical treatment, surgery and/or removal of the device however this is considered a rare circumstance. Electrical stimulation may increase tinnitus, facial nerve stimulation, balance related issues (such as dizziness or vertigo) or pain; implantation in the cochlea may preclude the use of future implant technology; and device failure of operation that may perhaps require removal of the device. It is important to note that the risk of removing a failed implant if necessary is considered to be minimal.

The aforementioned general risks and risks associated with implantation of the internal cochlear implant device and electrode array and external investigational devices are defined, described and provided in detail in the informed consent form template for study participants (Appendix B). All of these risks are anticipated.

Contraindications:

Deafness due to lesions of the acoustic nerve or central auditory pathway; active external or middle ear infections; cochlear ossification that prevents electrode insertion; absence of cochlear development; tympanic membrane perforations associated with recurrent middle ear infections.

Warnings:

Bacterial meningitis; extreme direct pressure on the implanted device up, down, left or right may cause the implant to move and possibly dislodge the electrode array; direct impact to the implant site may damage the implant and result in its failure to function; the long term effect of chronic electrical stimulation are unknown; electrode displacement can occur if the electrode is no inserted properly; electrosurgical instruments must not be used close to the implant or electrode. Electrosurgical instruments are capable of producing radio-frequency voltages that may cause damage to the cochlear tissues or permanent damage to the implant; diathermy must never be applied over the implant or electrode. High currents induced into the electrode can cause tissue damage to the cochlear or permanent damage to the implant; diagnostic ultrasound energy must not be used in the area of the implant; electroconvulsive therapy must never be used on a cochlear implant patient, it may cause tissue damage to the cochlea or permanent damage to the implant; ionizing radiation therapy cannot be used directly over the implant as it may damage the device; the effects of cobalt treatment and linear acceleration techniques on the implant are unknown; Magnetic Resonance Imaging Testing is conditions are outlined below, please contact Advanced Bionics Technical Support for additional information or reference the Instructions for Use for the respective product.

MRI safety information for HiRes 90K™ Advantage implants:

- MRI is contraindicated except under the circumstances described below. Do not allow patients with a HiRes 90K Advantage cochlear implant to be in the area of on MRI scanner unless the following conditions have been met:
    - The HiRes 90K Advantage is designed with a removable magnet to allow for MRI scans. The HiRes 90K Advantage is MRI safe at 0.3 Tesla and 1.5 Tesla. MRI safety at higher energy levels has not been tested.
    - The magnet must be surgically removed before lhe patient undergoes on MRI procedure.
    - Patients must also remove their sound processor and headpiece before entering a room where a MRI scanner is located.

MRI safety information for HiRes Ultra implants:

- Testing has demonstrated that the HiRes Ultra cochlear implant is MR Conditional. Unilateral and bilateral recipients with this device can be safely scanned in an MR system meeting the following conditions:

  3.0T with the magnet removed
    - The internal magnet must be removed. See the "*Surgeon Manual for the HiRes Ultra Cochlear Implant*" for removal instructions.
    - The external sound processor and headpiece are MR Unsafe and must be removed before entering a room containing an MR scanner.

  1.5T with the magnet in place
    - The external sound processor and headpiece are MR Unsafe and must be removed before entering a room containing an MR scanner.
    - A bandage must be applied using the bandaging protocol in the Instructions for Use.
        - Please note that the MRI Antenna Coil Cover, CI-7521, and bandaging supplies must be on hand at the time of the MRI procedure. Please contact Advanced Bionics technical support at [redacted] prior to the MRI procedure to request these supplies.
        - The bandaging protocol with use of the MRI Antenna Coil Cover was developed and approved to prevent magnet displacement and counteract magnet torque during a 1.5T MRI procedure, but some discomfort and pain at the implant site may still be experienced. Please consult with your physician if this is an issue.
        - Failure to secure the MRI Antenna Coil Cover and internal magnet in place during MRI may result in magnet displacement or the need for surgical revision.
- An MRI scan is not recommended if the patient has a fever

Precautions:

Electrostatic discharge can potentially damage sensitive electronic components such as the ones used in the cochlear implant system; digital cellular phones may cause interference with the cochlear implant system; airport/security metal detectors, x-ray machines and security scanners

will not damage the implant or sound processor, however, passing through security metal detectors may activate the detector alarm; implant user should only use his/her own sound processor that has been specifically programmed for them by their clinician; physical activity that include the possibility of trauma or impact, precautions should be taken, such as wearing a protective helmet, to reduce the risk of damage to the internal device.

The aforementioned general risks and risks associated with implantation of the internal cochlear implant device and electrode array are defined, described and provided in detail in the informed consent form template for study participants (Appendix B).

14.0 Ethical and Regulatory Obligations

14.1 Study Conduct

The Investigator must agree that the study will be conducted according to the protocol, the principles of Good Clinical Practices (GCPs) outlined in 21 CFR parts 50, 56, and 812, the World Medical Association Declaration of Helsinki, and internal Standard Operating Procedures (SOPs). In addition, the Investigator will conduct all aspects of this study in accordance with FDA and local regulations.

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

14.2 Institutional Review Board

Before initiation of the study, the Investigator must obtain approval of the research protocol, informed consent form, and subject recruitment materials from the governing IRB in compliance with the provisions specified by the FDA (21 CFR Part 56) and other applicable regulatory agencies. Although Advanced Bionics clinical research staff may assist with IRB applications, the Investigator is responsible for assuring compliance of the center's respective IRB with applicable regulations.

A copy of the written IRB approval of the protocol, informed consent, IRB application materials, and recruitment advertising (if applicable) must be provided to Advanced Bionics prior to initiation of the study. The approval letter must be signed by the IRB chairman or designee, specify the IRB name and address, identify the clinical protocol by title and/or protocol number, and include the date that approval was granted. The Investigator is responsible for obtaining continued review of the clinical study at intervals not exceeding one year or as otherwise specified by the IRB. The Investigator must provide Advanced Bionics with written documentation of the review and materials submitted to the IRB for continuing approval.

Investigators must notify the IRB promptly regarding all SAEs that occur at their site, in accordance with local reporting policy, and report other safety information provided by Advanced Bionics to the IRB.

14.3 Informed Consent

A study site's Informed Consent Form template with center specific/required language must be provided to Advanced Bionics for approval prior to submission to the Institutional Review Board (IRB). Advanced Bionics will provide an informed consent template and assistance in adapting that template to conform to local requirements (Appendix B). All informed consent documents and patient information sheets must contain the minimum elements as mandated by FDA (21 CFR Part 50) and will be subject to approval by Advanced Bionics as well as the IRB.

Before enrollment, the study will be explained to each prospective study candidate. Candidates will be asked to read the approved informed consent form 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 and date the informed consent form. The Investigator will provide a copy of the signed and dated informed consent form 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 informed consent form must be revised and submitted to the IRB for review and approval. Actively enrolled study participants are re-consented accordingly if affected by the amendment. The revised informed consent form 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.

14.4 Amendments and Deviations

14.4.1 Protocol Amendments

Any changes to the protocol must be implemented through a formal protocol amendment. Amendments to the protocol may be initiated by Advanced Bionics or at the request of the Investigator. In either case, a formal amendment cannot be initiated until it has been approved by Advanced Bionics, the Investigator, regulatory agencies (if applicable), and the IRB.

14.4.2 Emergency Deviations

Emergency deviations or modifications to the protocol may be initiated without Advanced Bionics or IRB approval (21 CFR 50.24) only in cases where an immediate apparent hazard to subjects must be avoided. Emergency deviations or modifications must be reported to Advanced Bionics and the IRB no later than 24 hours after the emergency.

14.4.3 Protocol Deviations

A protocol deviation refers to a study-related activity that is not in compliance with the approved investigational plan/protocol such as an assessment or part thereof are completed incorrectly or omitted or a participant not returning at a defined study interval. Deviation events are to be reported accordingly on a protocol deviation report form (CRF) in the Sponsor's Master binder. Deviations from the clinical protocol and protocol requirements including GCP guidelines will be reviewed and evaluated on an ongoing basis. Appropriate corrective actions

will be implemented as necessary. Dependent on nature of deviation, the Investigator may be required to notify the IRB.

15.0 Health Insurance Portability and Accountability Act (HIPAA)

All subjects must sign a HIPAA authorization form prior to participation in the study. The Investigator will prepare the HIPAA authorization form according to their institution's policy and provide it to Advanced Bionics for approval. Advanced Bionics will provide a template HIPAA research authorization form for reference. All subjects must sign the authorization form prior to participation in the study if the HIPAA information is not included in the institution's informed consent.

16.0 Study Monitoring

A clinical research monitor will supervise conduct of the study. 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 study site will assist the monitor by providing access to all relevant study materials.

17.0 Study Audits

Advanced Bionics' internal auditors or contract auditors may evaluate the conduct of the study. These parties will have access to all study-related documents. Advanced Bionics audit reports are confidential and proprietary.

18.0 Documents and Records

18.1 Pre-Study Documentation Requirements

Prior to obtaining consent from any subjects, the following documents are required:

- A copy of the protocol signature page, which serves as the Investigator Agreement, signed and dated by the designated study site Investigators (surgeons and audiologists)
- A signed and dated copy of the Clinical Trial Agreement with a completed Financial Disclosure for the Principal Investigator
- A copy of the IRB application and written IRB approval of the protocol
- A copy of the approved Informed Consent Form and written IRB approval of the form
- A copy of the signed and dated curriculum vitae of the Principal Investigator and Sub-Investigator(s), if applicable
- Copies of State licenses of the designated study site Investigators (surgeons and audiologists)

18.2 Study Documentation/Case Report Forms

Data must be submitted according to protocol requirements for all enrolled subjects. Electronic Case Report Forms (eCRFs) provided for this study will be used to submit data (Appendix A). Each subject will be assigned a unique identifier at the time of enrollment, which will be used on all eCRFs. Study records are comprised of source documents, eCRFs, and all other administrative documents including, for example, IRB correspondence, clinical trial materials and supplies shipment manifests, monitoring logs, and study-related correspondence with Advanced Bionics. 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 imaging, 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.

18.3 Device Accountability

Participants will be implanted and fit with the commercially available HiResolution™ Bionic Ear cochlear implant system (HiResolution™ system) at their respective hearing care/implant centers. The implant system will be shipped with the following label: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use." The internal cochlear implant device serial numbers will be logged at the study site for each study participant.

18.4 Record Retention

All study records (e.g., protocol, IRB correspondence and approvals, eCRFs, patient records, consent forms, reports) must be maintained 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 Advanced Bionics' approval and will be documented in writing with copies sent to Advanced Bionics. If an Investigator leaves the site at which the study was conducted, Advanced Bionics shall be contacted regarding the disposition of documents.

18.5 Inspection of Records

In the event of an audit, the Investigator agrees to allow representatives of the study Sponsor, FDA or other regulatory authorities to access all study records. Investigators should notify the study Sponsor promptly if an audit request is received from any regulatory or government agency. A copy of the audit findings if conducted should be forwarded to the study Sponsor following the conclusion of the visit.

19.0 Suspension and Termination

19.1 Criteria for Terminating the Study

The study Sponsor, Advanced Bionics, reserves the right to terminate the study at any time. However, this right will be exercised only for valid scientific or business reasons, or because of issues related to protection of research subjects. Investigators and IRBs will be notified in writing in the event of termination.

Results will be published on clinicaltrials.gov within 3 months of study termination, if the study is terminated due to unanticipated adverse device effects.

19.2 Criteria for Suspending or Terminating a Study Center

After the study begins, Advanced Bionics reserves the right to terminate enrollment of subjects at a study center at any time if (1) no subjects have been enrolled, (2) the center has multiple or severe unjustified protocol violations or (3) the center fails to follow remedial actions for protocol violations.

Possible reasons for suspending or terminating a center include:

- Investigator non-compliance.
- Repeated failure to complete or submit eCRFs in a timely manner.
- Failure to obtain written informed consent from each subject.
- Failure to report an SAE or UADE to Advanced Bionics within 10 days of when the event occurred.

19.3 Investigator Responsibilities

Investigators participating in this study must agree:

- Sign, adhere and conduct the study in accordance with the approved investigational plan, the Clinical Trial Agreement, FDA regulations and conditions of approval set forth by the Institutional Review Board or the FDA
- To provide a signed and dated copy of their curriculum vitae
- To obtain IRB approval of the study protocol and secure continuing review and approval of the study until it is closed.
- To supervise all testing of human subjects.
- To ensure that informed consent is properly obtained for all subjects
- To not release any details of the study without the prior written consent of Advanced Bionics except for presentation/publication of results in a scientific forum in accordance with the Clinical Trial Agreement.
- That decision on authorship, timing, and content of publications and presentations from the study will be conducted in accordance with the Clinical Trial Agreement.

20.0 Monitoring Procedures

Independent monitoring of the feasibility study for clinical protocol compliance will be conducted periodically to oversee compliance with the regulatory and clinical aspects of the study. The Clinical Monitor will maintain current knowledge of the study through observation, review of study records and source documentation, and discussion of the study with the investigators and delegated study personnel.

Clinical Monitors will be members of the Clinical Research, O.R. Support or Technical Services Departments of Advanced Bionics who have been trained on the study investigational plan, monitoring procedures, and standard operating procedures based on Good Clinical Practice and other applicable Federal regulations.

The following or otherwise designated Advanced Bionics Clinical Research Department Personnel will be responsible for conducting the feasibility study monitoring:

Name, telephone number(s) and email address:

[redacted]

Address:

Advanced Bionics, LLC
Clinical Research Department
28515 Westinghouse Place
Valencia, CA 91355
[redacted]

20.1 Site Initiation Training

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

- Good Clinical Practice, including investigator responsibilities and purpose of monitoring activities
- Requirements for IRB approval (initial application and continuing reviews)
- Informed consent procedures, including requirements for inclusion of all foreseeable risks in the informed consent form
- Study investigational plan and procedures (technical information on use of the investigational product may be reviewed by members Technical Services Departments, if appropriate)
- Processes for recording and reporting adverse events
- Device accountability procedures
- Data collection and correction procedures, source documentation, and record retention requirements

20.2 Interim Monitoring Activities

The Clinical Monitor will perform the following activities during study monitoring:

- 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 informed consent forms for completeness and accuracy
- Confirm that the study investigational plan is being followed and that any changes in the protocol have been reported to the IRB as applicable
- Review eCRFs and source documents for completeness, accuracy, and timely submission to Advanced Bionics
- Collect outstanding eCRFs
- Verify that all adverse events have been reported 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 eCRF and submit within the required timeframe
- Review and resolve queries, if appropriate
- Review device accountability records
- Ensure that any investigational product is stored in a secure location if applicable to study
- Follow up on outstanding monitoring visit action items

At the end of each interim monitoring visit, the Clinical Monitor will meet with the investigators to review site compliance with the study investigational plan, investigator responsibilities, and applicable regulations.

20.3 Close-Out Monitoring Activities

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

- Conduct review and collection of regulatory documents
- Resolve open queries
- Review study file retention and storage requirements
- Collect outstanding CRFs
- Review investigator responsibilities including IRB notification of study closure
- Follow up on any outstanding issues, including unresolved adverse events
- Review the potential of regulatory or Sponsor audits
- Return any unused investigational product to Advanced Bionics if applicable to study

At the end of the close-out visit, the Clinical Monitor will meet with the investigators to review site compliance with the study investigational plan, investigator responsibilities, and applicable regulations.

20.4 Management of Site Noncompliance

Observations of noncompliance with the study investigational plan, regulatory requirements, or any conditions of approval imposed by the IRB or the FDA 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, Advanced Bionics will stop shipping investigational product and request that any investigational product at the site be returned.

20.5 Documentation and Records

The Study Sponsor, Advanced Bionics, maintains files with regulatory documents (study investigational plan, IRB approval and sample informed consent form, investigator agreement, CVs, monitor reports). Electronic CRFs are completed for each study subject. The Sponsor maintains the original eCRFs.

The Clinical Monitor documents monitoring activities, including training activities, telephone conversations, and e-mail correspondence on designated study logs and forms. A report is completed after each monitoring visit that includes the date of the visit, name and address of investigator, statement of the findings, conclusions, and any actions taken by the Monitor and/or investigator to correct deficiencies or conditions of noncompliance with the investigational protocol or regulatory requirements. A report or a follow-up letter summarizing the monitoring activities, including follow-up action items and corrective actions to resolve deficiencies, if appropriate, are kept on file in the study regulatory binder on-site at Advanced Bionics.

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22.0 Protocol Amendments

In the event of an amended change to the feasibility study protocol, the Sponsor will submit accordingly to the FDA for review/approval. Amended changes will be provided as well for Institutional Review Board submission and review.

23.0 Study Site and Investigator(s)