Implantation of the HiRes90K™ Advantage Cochlear Implant with HiFocus™ Mid-Scala and Development of a Combined Electric and Acoustic Stimulation Technology in Adults with Partial Deafness

INVESTIGATIONAL PLAN
FEASIBILITY IDE

26 September 2016

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1.0 Investigator Signature Page

Study Title:	Implantation of the HiRes90K™ Advantage Cochlear Implant with HiFocus™ Mid-Scala and Development of a Combined Electric and Acoustic Stimulation Technology in Adults with Partial Deafness
Study Center:	Center Name Address Phone Fax

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 _____

Printed Name of Investigator _____

Date: _____

2.0 Protocol Synopsis

Study Title	Implantation of the HiRes90K™ Advantage Cochlear Implant with HiFocus™ Mid-Scala and Development of a Combined Electric and Acoustic Stimulation Technology in Adults with Partial Deafness
Sponsor	Advanced Bionics, LLC
Device	HiRes 90K™ Advantage implant with HiFocus™ Mid-Scala electrode Sound Processor(s): Commercial Advanced Bionics Cochlear Implant Sound Processor / Prototype Advanced Bionics EAS Cochlear Implant Sound Processor and EAS Earhook
Primary Study Objective	To implant and fit patients with considerable low-frequency acoustic hearing profiles (partial deafness) with the Bionic Ear System (HiRes 90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode) and prototype Advanced Bionics EAS Cochlear Implant Sound Processor to complete the development of Advanced Bionics electro-acoustic stimulation technology.
Study Design	The primary purpose of this study is to allow Advanced Bionics to complete the development of its' electro-acoustic stimulation technology. As part of this study, individual outcomes (for the newly implanted group) will be compared across pre and postoperative test conditions for the audiometric threshold outcomes. Prospective within-subjects repeated-measures design, each subject serves as his/her own control
Study Population	Up to 35 newly implanted adults (this is up to an additional 25 newly implanted adults to the original N=10 recruited under initial study approval);Up to 20 participating U.S. study sites;); 15 existing implanted adults total (recruited from participating U.S. study sites). Total possible number of feasibility study participants (newly implanted and existing groups) N=50.
Primary Efficacy Objective	As the purpose of this study is to complete technology development, the collection of efficacy data to support product approval is not part of this study. Efficacy will be studied and proven in a separate pivotal study, once the technology development is completed. As part of this study, some audiometric data will be collected.
Safety Objective	As the purpose of this study is to complete technology development, the collection of safety data to support product approval is not part of this study. Safety will be studied and proven in a separate pivotal study, once the technology development is completed. As part of this study, adverse events will be tracked and reported to ensure that the safety of patients is maintained.
Inclusion Criteria: Newly Implanted Group	• Ability to provide informed consent • No previous cochlear implant experience *in either ear* • 18 years of age or older • Up to a moderate sensorineural hearing loss in the low-to-mid frequencies (pure tone average ≤ 65 dB for 125, 250, 500, and 1000 Hz) and a severe-to-profound sensorineural hearing loss in the high

	frequencies (pure tone average ≥ 70 dB HL for 2,000, 3000, 4,000, and 8,000 Hz) in the *ear to be implanted* • Aided CNC word recognition score up to 50% in *ear to be implanted* • Up to a moderate sensorineural hearing loss in the low-to-mid frequencies (pure tone average ≤65 dB for 125, 250, 500, and 1000 Hz) and a severe-to-profound sensorineural hearing loss in the high frequencies (pure tone average ≥ 70 dB HL for 2,000, 3000, 4,000, and 8,000 Hz) in the *contralateral (non-implanted) ear* • Aided CNC word recognition score up to 80% in the *contralateral (non-implanted) ear* • English language proficiency • Willingness to use an ear-level sound processor postoperatively for the duration of the study trial • Willingness to participate in all scheduled procedures outlined in the protocol
Exclusion Criteria Newly Implanted Group	• Preoperative audiometric conductive overlay of 15 dB or greater at two frequencies or more in range of 500-1000 Hz *in the ear to be implanted* • Congenital hearing loss (for purpose of this study, onset prior to age 2 years*) • Duration greater than 30 years of severe-to-profound high-frequency hearing loss • Cochlear malformation or obstruction 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 • Deafness due to central auditory lesion or cochlear nerve deficiency, 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 **Based on critical period for speech and language development*
EAS Fitting Inclusion Criteria: Newly Implanted and Existing Implanted Group	• Ability to provide informed consent • 18 years of age or older, *unilaterally implanted* with HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode and fit with an ear-level sound processor (i.e. Naída family device) • Postoperative unaided low frequency audiometric hearing thresholds in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz • English Language Proficiency • Willingness to participate in all scheduled procedures outlined in the study protocol
EAS Fitting Exclusion	• *Unilaterally implanted with* HiRes 90K™ Advantage cochlear implant

Criteria Newly Implanted and Existing Implanted Group	with HiFocus™ Helix® and/or HiFocus™ 1j electrode • Exclusive use of a body worn external sound processor • Deafness due to central auditory lesion or cochlear nerve deficiency, diagnosis of auditory neuropathy/dys-synchrony *in either the implanted or the contralateral ear* • Postoperative unaided low frequency audiometric hearing thresholds in the treated ear exceeding 80 dB HL at each frequency from 125 – 1000 Hz • Unwillingness or inability of subject to comply with all investigational requirements as determined by the investigator
Efficacy Endpoints	Unaided pure tone hearing threshold measurement in the treated ear compared to preimplant audiometric thresholds (using pure-tone average of .125, .25, .5 and 1 kHz for comparison) as these relate to the device parameter settings for the combined delivery of electric-acoustic stimulation to the treated ear; speech perception measures in quiet and sentence recognition in noise pre to post device activation will be compared; Speech, Spatial Qualities (SSQ), Abbreviated Profile of Hearing Aid Benefit (APHAB) and Sponsor developed patient questionnaire comparison pre- to-post device activation to provide a subjective measure of patient perceived hearing performance/auditory benefit with this technology
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.
Efficacy Evaluations	The collection of efficacy data to support product approval is not part of this feasibility study. Pre-to-postoperative comparisons of: unaided audiometric hearing thresholds (using pure-tone average .125, .25, .5 and 1 kHz); monosyllabic word and sentence recognition performance in quiet and noise conditions and subjective measure of perceived benefit using SSQ, APHAB and Sponsor developed metrics 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 Schedule	*Newly Implanted Group* • Consent: Subject will sign Informed Consent document prior to conduct of any study procedures • Baseline: Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing ; Patient Questionnaire completion (Speech, Spatial Qualities SSQ metric; Abbreviated Profile of Hearing Aid Benefit APHAB; Sponsor developed patient report questionnaire) • Implant Surgery (to occur within 12 weeks of Baseline test interval):

	Surgical Questionnaire completed by surgeon at time of implantation • Initial Device fitting (to occur within 3-6 weeks postimplantation) ; collection of tympanometry; unaided audiometric testing; fitting and programming of the commercial AB cochlear implant sound processor (treated ear); aided audiometric testing • 1 Week post initial device fitting (to occur within 7-10 days from initial device fitting date): Tympanometry; unaided audiometric testing ; adjustment / optimization of program parameters as recommended by managing clinician • 1 Month post initial device fitting (to occur within 4 weeks (+/- 7 days) from the initial device fitting date): Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing; SSQ, APHAB, Sponsor developed Patient Report questionnaires; adjustment / optimization of program parameters (for subject's owned commercial device) as recommended by managing clinician; AB prototype ***EAS*** (combined acoustic + electric input) sound processor and earhook *fitting** and programming (*for subjects meeting residual hearing inclusion criteria in the implanted ear); aided and bilateral listening speech perception testing with EAS device; Sponsor developed Usability Questionnaire • 2 Months post initial device fitting (1 month post EAS device fitting): Visit to occur within 4 weeks from the 1 month post initial device fitting test interval visit (+/- 7 days): Tympanometry; unaided and aided audiometric testing; bilateral listening condition only speech perception testing ; SSQ, APHAB, Sponsor developed Patient Report and Usability Questionnaires; adjustment / optimization of program parameters as recommended by managing clinician (for subject's owned commercial device and/or EAS device) • 3, 6 and 12 Months post *initial* device fitting (to occur within 12, 24 and 48 weeks respectively from the initial device fitting date (+/- 14 days): Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing ; SSQ, APHAB, Sponsor developed Patient Report and Usability Questionnaires; adjustment / optimization of program parameters as recommended by managing clinician (for subject's owned AB commercial device and/or EAS device) EAS Extended Use Arm – Optional: • 24, 36, 48, etc. Months post initial device fitting (to occur within 96, 144 and 192, etc. weeks, respectively, from initial device fitting (+/- 8 weeks): unaided low-frequency audiometric testing – treated ear; aided listening condition speech perception testing – treated ear; Sponsor developed Usability Questionnaires; adjustment / optimization of program parameters as recommended by managing clinician (for subject's EAS device) • Termination Visit (to occur at the point of EAS discontinuation by patient/clinician, or to occur within 12 weeks of full EAS

	commercialization): unaided low-frequency audiometric testing – treated ear; aided listening condition speech perception testing – treated ear; Sponsor developed Usability Questionnaires *EAS Fitting Study Schedule for Existing Implanted Group* • *Initial* Visit (Baseline Assessment) and EAS device fitting: Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing (using subject's AB owned commercial device) ; AB ***EAS*** *prototype* (combined acoustic + electric input) sound processor and earhook *fitting** / programming; aided and bilateral listening condition speech perception testing (using EAS device); SSQ, APHAB, Sponsor developed Patient Report and Usability Questionnaires • 1 Month post *EAS* device fitting: Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing; SSQ, APHAB, Sponsor developed Patient Report and Usability Questionnaires; adjustment /optimization of program parameters for subject's owned AB commercial device and/or EAS device as recommended by managing clinician • 3, 6, 12 Months post *EAS* device fitting: Tympanometry; unaided and aided audiometric testing; aided and bilateral listening condition speech perception testing ; SSQ, APHAB, Sponsor developed Patient Report and Usability Questionnaires; adjustment / optimization of program parameters for subject's owned AB commercial device and/or EAS device as recommended by managing clinician EAS Extended Use Arm - Optional: • 24, 36, 48, etc. Months post initial EAS fitting (to occur within 96, 144 and 192, etc. weeks, respectively, from initial EAS fitting (+/- 8 weeks): unaided low-frequency audiometric testing – treated ear; aided listening condition speech perception testing – treated ear; Sponsor developed Usability Questionnaires; adjustment / optimization of program parameters as recommended by managing clinician (for subject's EAS device) • Termination Visit (to occur at the point of EAS discontinuation by patient/clinician, or to occur within 12 weeks of full EAS commercialization): unaided low-frequency audiometric testing – treated ear; aided listening condition speech perception testing – treated ear; Sponsor developed Usability Questionnaires
Study Monitoring	Advanced Bionics, LLC 28515 Westinghouse Place Valencia, CA 91355 [redacted]
Data Consulting	CROS NT LLC 501 Eastowne Drive, Suite 230 Chapel Hill, NC 27514 [redacted]

3.0 Glossary

Study Term	Definition
Partial Deafness	Hearing Loss configuration with considerable low frequency acoustic hearing and severe-to-profound high frequency sensorineural hearing loss
Functional Residual Hearing	Unaided acoustic hearing thresholds (in dB HL) sufficient to be aided with conventional amplification (≤80 dB HL)
Electric-Acoustic Stimulation (EAS)	Combined delivery of electric and acoustic stimulation
Preferred Listening Program	Postoperatively used to refer to a participant's preferred implant sound processor program (electric only and/or EAS (electric+acoustic program)
Everyday Listening Condition	This is used within this study protocol to refer to a participants' typical listening condition (binaural hearing – both ears). As this population has partial deafness; participants may or may not utilize amplification in one of the ears as low frequency acoustic input may be sufficient and/or not require use. Thus, for purposes of this study, notation is provided with respect to the 'bilateral listening condition' testing, defined below, to account for the possibility of varied everyday listening conditions for study participants
Bilateral Listening Condition	For purposes of this study, bilateral listening condition refers to a participant's *everyday* listening condition (with both ears – defined above). Preoperatively: acoustic hearing condition for both ears (with or without amplification); Postoperatively: cochlear implant alone in one ear + acoustic hearing (with or without amplification) in opposite ear; combined electric+acoustic (EAS) hearing in implanted ear + acoustic hearing (with or without amplification) in opposite ear

4.0 Purpose of the Investigation

The HiResolution™ Bionic Ear cochlear implant system is 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.

The purpose of the proposed feasibility study is to evaluate whether low-frequency acoustic hearing sensitivity can be preserved in newly implanted adults with partial deafness (considerable low frequency acoustic hearing profiles with severe-to-profound high frequency sensorineural hearing loss) using the HiResolution™ 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode to support the development of electro-acoustic stimulation technology. A feasibility study approach will additionally provide basic, valuable aspects of device safety and functionality prior to an initiation of a pivotal study and aid to establish appropriate endpoints and outcome measures for such a study.

There are two groups of study participants that will be recruited for the feasibility study to support the development of electro-acoustic stimulation technology for a partial deafness population: a newly implanted group and an existing implanted group.

Recruitment and implantation of a newly implanted group of participants with partial deafness using the HiRes 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode carrier provides preliminary outcomes and insight as to the preservation and/or contribution of low-frequency acoustic residual hearing in the treated ear following receipt of this treatment. Participants will be implanted with the HiRes 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode unilaterally and fit initially with a currently commercially available Advanced Bionics (AB) cochlear implant external sound processor using the commercially available custom fitting software, SoundWave™ Professional Suite. As the Sponsor is working to complete the development of a combined delivery sound processor to provide both acoustic and electric stimulation (EAS), a prototype Advanced Bionics EAS cochlear implant (CI) Sound Processor with EAS Earhook will be used and fitted to participants postimplantation that meet the EAS fitting criterion defined within the study protocol. EAS fitting for these patients is to occur at the respective managing study center at the 1 month post initial device activation visit for newly implanted participants, and at the Baseline visit for existing implanted participants. Existing implanted group participants meeting the study inclusion criteria will be fit, programmed and assessed at scheduled test intervals at the respective managing study center.

Participants completing the 12 month study test interval for the EAS feasibility study may be invited for participation in additional studies at the Sponsor's headquarters in Valencia, California.

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(s)) at the time of implantation. The HiResolution™

Bionic Ear cochlear implant system consists of (1) an externally worn sound processor; (2) internal components consisting of an implantable electronics package and electrode (HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode); and 3) a custom fitting software used to program the external sound processor.

Internal Device (HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode):
The commercially available HiRes 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode will be used in the study. The HiFocus™ Mid-Scala electrode consists of a 16 platinum contacts, each connected to a platinum/iridium contact wire. The stimulating contacts and contact wires are enclosed in a silicone carrier. The total length of the array is 18.5 mm, thereby enabling an approximate angular insertion depth of 420 degrees (approximately 1¼ cochlear turns).

The electrode carrier is designed to allow surgeons the flexibility to use varying surgical approaches and techniques (i.e. cochleostomy or round window approach depending on surgeon's experience, preference and patient cochlear anatomy) that have been shown to enable easy insertion and aim to protect the delicate structures of the cochlea (Briggs et al. 2005; Friedland and Runge 2009; Skarzynski et al. 2002; 2007b; Adunka et al. 2004b; Adunka et al. 2006; von Ilberg et al. 1999; Keifer et al. 2004; Roland et al. 2007; Gantz and Turner 2003; Gstoettner et al. 2004; 2009). For added flexibility, the electrode is delivered pre-loaded onto a stylet and can be inserted with or without a disposable insertion tool. The tool has been designed to provide optimal visualization of the cochlea and electrode trajectory and effectively offers the surgeon a free-hand (off-stylet) insertion technique. A spare stylet and reloading tool are available. This allows the electrode to be reloaded up to two times, facilitating three insertion attempts. With these options and flexibility, surgeons can use the surgical approach—with or without the tool—that is determined preferable.

External Device / Software:
Newly implanted participants will be initially fit and programmed (electric stimulation only) with his/her commercial ear-level (i.e. Naída family) Advanced Bionics cochlear implant sound processor (as part of the HiResolution™ Bionic Ear cochlear implant system prior to implantation) with conventional earhook or T-mic for the treated ear following implant surgery. Method of fitting (software and coding strategy) will be completed by the patient's managing hearing care provider using the commercially available programming software, SoundWave™ Professional Suite and the Clinicians Programming Interface (CPI).

Electric Acoustic Stimulation (EAS) Device Fitting:
The proposed feasibility study is intended to evaluate and complete the development of the hardware and software which combines electric and acoustic (EAS) technologies. As the Sponsor is working to complete the development of the electric-acoustic stimulation technology; participants qualifying for the EAS fitting aspect of the feasibility study will be fit at the managing hearing care center 1 month post device activation (for newly implanted group participants) and at the Baseline visit (for existing implanted participants) with an Advanced Bionics EAS prototype cochlear implant sound processor and EAS Earhook. The device(s) will be programmed using an investigational version of the commercial programming software and interface (SoundWave™ Professional Suite with EAS programming capability and respective Clinician's Programming Interface) supporting the EAS device to provide the delivery of the combined sound input of acoustic plus electric stimulation.

A description of the investigational device and components is provided in the sections below. Minor changes to the investigational device and/or components can be reasonably expected to occur, and will be used to iterate the design concept based upon the patient feedback. These changes will not require a 5 Day Notice to FDA as they are expected to occur and do not affect patient safety. It is important to note that there shall be no changes made to the cochlear implant or to any of the controls that ensure patient safety.

Any change which does affect patient safety shall not be implemented before approval is obtained from the FDA. All changes will be made in accordance with the Advanced Bionics Quality System.

5.1.2 Prototype Cochlear Implant Sound Processor

Newly implanted or existing implanted group participants meeting the EAS fitting inclusion criteria will be fit with an Advanced Bionics (AB) prototype cochlear implant sound processor capable of delivering combined electric and acoustic stimulation (EAS). The sound processor will be coupled (physically connected) with an acoustic receiver module (EAS earhook-refer to description and Figure 1 below), in place of a conventional earhook or T-Mic, capable of amplifying low frequency sounds for individuals with functional residual hearing following cochlear implantation. It is anticipated in the development of a new cochlear implant sound processor, during the course of the study the following may occur:

- Design modifications to molded materials (e.g. plastic, rubber, silicone or Teflon) to address cosmetic issues (e.g. mold flash or mold sink) or to incorporate suggested improvements.
- Substitution of one biocompatible material for another biocompatible material of a different grade with respect to particular mechanical properties (e.g. sheer strength, impact strength) to improve reliability, yields or cosmetics. (*Note: The molded materials are known biocompatible materials for which Advanced Bionics has ISO 10993 test results on file).*
- Changes to printed circuit board assembly process or design to incorporate improvements in manufacturability, yield or cost.
- Changes to printed circuit board assembly process or design to incorporate functionally equivalent replacements for obsolete components.
- Changes in circuit topology to reduce power consumption, individual physical component size or final assembly size of electromechanical subsystems. This will result in a smaller physical size for improved patient ease of use and aesthetic improvements.

5.1.3 EAS Earhook Device

The earhook hardware shall consist of a canal receiver leveraged from commercially available Phonak Canal Receiver hearing instrument Technology (CRT) that is physically connected to and used in conjunction with a compatible Advanced Bionics (AB) prototype sound processor to provide both acoustic and electric stimulation to the same ear. Design changes incorporated

through the evaluation of an EAS earhook may address issues of sound preference, performance, reliability or cosmetics, and ease of use.

The types of changes anticipated to occur during development of the EAS Earhook are:

- Design modifications to molded materials (e.g. plastic, rubber, silicone or Teflon) to address cosmetic issues (e.g. mold flash or mold sink) or to incorporate suggested improvements.
- Substitution of one biocompatible material for another biocompatible material of a different grade with respect to particular mechanical properties (e.g. sheer strength, impact strength) to improve reliability, yields or cosmetics. *Note: The molded materials are known biocompatible materials for which Advanced Bionics has ISO 10993 test results on file.*

Figure 1 – EAS Earhook Mechanical Mockup

5.1.4 EAS Supporting Software

SoundWave™ investigational software supporting the EAS device to provide the delivery of the combined sound input of acoustic plus electric stimulation will be used during the feasibility study. The software and respective platform for setting the device will aid in determining whether changes in stimulation and fitting result in improvements in terms of performance, self-reported quality, clarity, preference, detection, discrimination, speech perception, and ease-of-use. Investigators will also explore the relationship between acoustic and electric frequency representations. It is important to note that these studies involve modifications to all aspects of software, but none of the changes will modify the parameters and operational principles governing stimulation safety (e.g., charge-balanced stimulation, charge density limits, current density limits, etc.) nor will there be a development of a new sound coding strategy during this feasibility study. Full, bench-level safety testing of all software modifications will be done in all

cases prior to patient application to minimize patient risk. All of the designs to be evaluated are based upon devices approved under P960058 Harmony HiResolution Bionic Ear System.

To evaluate the benefits of the combined sound stimulation delivery (electric and acoustic) participants may be tested using a variety of programs with each feature independently (i.e. electric only or acoustic only or combined).

The types of software changes anticipated to occur during the software development for EAS stimulation in this study are:
Acoustic and electric frequency allocations/settings
Software bug fixes intended to correct software or user-interface functionality
User interface enhancements
Workflow changes

6.0 Study Objectives

The primary objective of the feasibility study is to evaluate whether *functional* low-frequency acoustic hearing sensitivity can be retained in newly implanted adults with partial deafness (considerable low frequency acoustic hearing profiles with severe-to-profound high frequency sensorineural hearing loss) following the implantation of the HiResolution™ 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode to further support the development and completion of the Advanced Bionics electro-acoustic stimulation (EAS) technology. Functional hearing is defined as unaided acoustic hearing thresholds (in dB HL) sufficient to be aided with conventional amplification (≤80 dB HL). For purposes of this study, the specific criteria to be used is postoperative unaided low frequency audiometric thresholds in the treated ear up to 80 dB HL for at least one frequency from 125-1000 Hz.

There are two groups of study participants that will be recruited for the feasibility study to support the development of electro-acoustic stimulation technology for a partial deafness population: a newly implanted group and an existing implanted group. Each participant group will complete a 12 month test study endpoint visit. Each participant group will have the option to enroll in an EAS Extended Use Arm at the discretion of the managing clinician and the subject. The EAS Extended Use Arm is optional and will provide access to the investigational EAS device up until the point of full commercialization.

Assessment of each participant group (newly and existing implanted groups) will last a minimum of approximately 15-19 months, and will assess the level of residual acoustic hearing (by measurement of audiometric thresholds) and speech understanding performance in the treated ear (and bilateral listening condition) throughout the study.
Newly implanted study participants who demonstrate and meet the functional preservation of hearing post-implantation (by measurement of audiometric thresholds) at the one month post device activation visit at the participating study sites will be fit with the AB prototype EAS sound processor at his/her managing hearing care center. A more acute fitting postimplantation is beneficial to gain further understanding and insight in evaluating the effects and abilities of perceptual order with various arrays of inputs (acoustic and electric input to an auditory pathway), the time to integration and acclimatization assessed using various outcome measures.

Existing implanted study participants identified and recruited at the participating study centers will also be fit with the prototype EAS device at his/her managing hearing care center. The Sponsor believes it is important in an existing implanted group to also gain insight as to the integration of acoustic and electric frequency representation, sound quality and listening preference. Existing implanted study participants recruited for the study may have been implanted off label on their own accord or through another investigational study. 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. Finally it is helpful to gain insight into fitting preferences and ease of use in software from hearing care specialists when simultaneously programming electric and acoustic stimulation in a partially deafened clinical population implanted with the Advanced Bionics System. The Sponsor intends to request feedback from the managing hearing care specialists from the participating centers throughout the study period to gain this insight.

All device-related and non-device-related adverse events will be tracked and reported accordingly through the 12 Months Post Initial Device Fitting Visit. Device-related or procedure-related adverse events will be reported throughout the EAS Extended Use Arm.

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 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 complete technology development for the combined sound delivery of electric and acoustic stimulation (EAS) to the treated ear. The collection of efficacy data to support product approval is not part of this feasibility study. However, as part of this feasibility, some audiometric, speech performance and subjective outcome data will be collected.

Specifically, for the newly implanted group: audiometric threshold measures at various, defined postoperative test intervals in the treated ear will be collected and compared to preimplant audiometric thresholds (using pure-tone average of .125, .25, .5 and 1kHz for comparison) . Measures of speech understanding and subjective outcomes will also be collected. Specifically,

collection of monosyllabic word recognition performance in quiet using the CNC word test and sentence recognition in noise using AzBio sentence test pre- to-post device activation will be compared for the newly implanted group. The Speech, Spatial Qualities (SSQ), Abbreviated Profile of Hearing Aid Benefit (APHAB), and Sponsor developed patient questionnaire(s) will be compared pre-to-post device activation to provide a subjective measure of patient perceived hearing performance/auditory benefit with this combined technology.

Audiometric, speech performance and subjective assessments will be additionally administered and evaluated for the existing implanted group participants enrolled in the feasibility study in an effort to gain insight with respect to EAS technology and postimplant performance. The Sponsor will make efforts to request preimplant hearing threshold data for the existing implanted group of participants in an attempt to evaluate and offer further insight as to the level of acoustic hearing preservation postimplantation with the Mid-Scala electrode array. These records for existing implanted participants may or may not be available to the managing clinical center and/or study Sponsor; however, the attempt at retrieval of this information will be made.

7.2.2 Safety

As part of this study, data (adverse event) will be collected and evaluated to ensure that the safety of patients is maintained accordingly as per requirements of an IDE and respective center Institutional Review Board guidelines for reporting.

7.3 Study Duration

The participant's study endpoint for the feasibility study is following completion of the twelve month test interval. It is expected that study participation for a subject enrolled in the feasibility study will involve a minimum 15-19 month commitment allowing for all scheduled test intervals and assessments.

The number of subjects proposed for recruitment in this feasibility study is estimated to be large enough to allow for trend analyses and to provide data suitable to support and complete product development.

7.4 General Subject Population

Projected total study enrollment under this feasibility study is 50 subjects. The Sponsor expects to add to current study recruitment and implant up to an additional 25 adult subjects across 20 study sites in the United States and recruit 15 existing implanted subjects with HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode. The additional 25 subjects for the newly implanted group is additive to the original N=10 subjects (based on initial FDA study approval), thus 35 newly implanted subjects are to be recruited. The existing implanted group of subjects to recruit remains (N=15).

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 (IRBs). Study participants are required to meet the study inclusion criteria (provided below) as determined by respective medical/hearing care providers. All consented participants meeting

criteria for the newly implanted group will be implanted with the commercially available HiResolution Bionic Ear Cochlear Implant System with the HiRes 90K™ Advantage implant with HiFocus™ Mid-Scala electrode and fit with a currently commercial ear-level (i.e. Naída family) Advanced Bionics 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. Existing implanted study participants recruited for the study may have been implanted off label on their own accord or through another investigational study.

7.5 Newly Implanted Group Inclusion and Exclusion Criteria

Inclusion criteria:

- Ability to provide informed consent
- No previous cochlear implant experience *in either ear*
- 18 years of age or older
- Up to a moderate sensorineural hearing loss in the low-to-mid frequencies (pure tone average ≤65 dB for 125, 250, 500, and 1000 Hz) and a severe-to-profound sensorineural hearing loss in the high frequencies (pure tone average ≥ 70 dB HL for 2,000, 3000, 4,000, and 8,000 Hz) in the *ear to be implanted*
- Aided CNC word recognition score up to 50% in *ear to be implanted*
- Up to a moderate sensorineural hearing loss in the low-to-mid frequencies (pure tone average ≤65 dB for 125, 250, 500, and 1000 Hz) and a severe-to-profound sensorineural hearing loss in the high frequencies (pure tone average ≥ 70 dB HL for 2,000, 3000, 4,000, and 8,000 Hz) in the *contralateral (non-implanted) ear*
- Aided CNC word recognition score up to 80% in the *contralateral ear*
- English language proficiency
- Willingness to use an ear-level sound processor postoperatively for the duration of the study trial
- Willingness to participate in all scheduled procedures outlined in the protocol

Exclusion Criteria:

- Preoperative audiometric conductive overlay of 15 dB or greater at two frequencies or more in range of 500-1000 Hz *in the ear to be implanted*
- Congenital hearing loss (for purpose of this study, onset prior to age 2 years*)
- Duration greater than 30 years of severe-to-profound high-frequency hearing loss
- Cochlear malformation or obstruction 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
- Deafness due to central auditory lesion or cochlear nerve deficiency, 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

**Based on critical period for speech and language development*

EAS Fitting Inclusion Criteria: ***Newly Implanted and Existing Implanted Groups***

- Ability to provide informed consent
- 18 years of age or older, *unilaterally implanted* with HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode and fit with an ear-level sound processor (i.e. Naída family device)
- Postoperative unaided low frequency audiometric hearing thresholds in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz
- English Language Proficiency
- Willingness to participate in all scheduled procedures outlined in the study protocol

EAS Fitting Exclusion Criteria:

- *Unilaterally implanted with* HiRes 90K™ Advantage cochlear implant with HiFocus™ Helix® and HiFocus™ 1j electrode
- Exclusive use of a body worn external sound processor
- Deafness due to central auditory lesion or cochlear nerve deficiency, diagnosis of auditory neuropathy/dys-synchrony *in either the implanted or the contralateral ear*
- Postoperative unaided low frequency audiometric hearing thresholds in the treated ear exceeding 80 dB HL at each frequency from 125 – 1000 Hz Unwillingness or inability of subject to comply with all investigational requirements as determined by the investigator

7.6 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
- Failure to attend, provide required testing, feedback or documentation for a respective follow-up visit after three documented attempts to contact the subject

Participants who withdraw or who are discontinued from the study will be reported accordingly to the study Sponsor and the study center's Institutional Review Board in accordance to respective guidelines. 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 hearing-impaired patient populations at the participating study sites. A participant's willingness and ability to meet the follow-up requirements will be determined by the investigator and informed consent will be obtained. A signed and dated informed consent will be kept in the participant's study record at the study site and copy provided to the participant accordingly. 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 Exhibit 2, Attachment 2.3, Appendix C 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 to determine if they meet 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 Measures

Primary Test Measures Used in Feasibility:
For the newly implanted group: the CNC monosyllabic word test will be used as the primary test metric for determination of preimplant candidacy. In addition to the primary metric, AzBio Sentences in Noise will be administered preoperatively for the ear to be treated (implanted) and in a bilateral listening condition. Postoperatively, for both the enrolled newly implant group and the existing implant participant group, CNC words in quiet and AzBio Sentences in Noise will be evaluated for both the treated ear and in the participant's bilateral listening condition.

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

8.3.1 Audiometric Measures:

Unaided air and bone conduction hearing thresholds (in dB HL) will be measured for each ear using the standard audiometric technique for pure-tone air and bone-conduction testing (refer to Exhibit 2, Attachment 2.3, Appendix A for the speech testing guidelines). Given the clinical population for which this feasibility study is evaluating (partial deafness), standard audiometric clinical masking procedures are applied as necessary to reduce any potential contribution of the better hearing ear during pre and postimplant assessments.

- Tympanometry (226 Hz)
- Unaided air conduction thresholds using insert earphones at octave and inter-octave frequencies will be obtained (125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz)
- Unaided bone-conduction hearing thresholds for the frequencies 250, 500, 1000, 2000, 3000 and 4000 Hz will be measured
- Aided warble-tone soundfield testing for the frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz

Note: Clinician will need to confirm the study participant's response to any pure tone stimulus presented at 125 and 250 Hz as auditory "heard" versus vibrotactile "felt" and record the response accordingly. Postoperatively, if no measurable hearing at the limits of the test equipment is documented at 2 consecutive visits, unaided audiometric testing for the TREATED ear does not need to be completed.

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 (ANSI) and/or Manufacturer Specifications.

Speech perception measures 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 dBA. 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). Preoperatively, participants are tested in the defined 'aided' conditions using his/her hearing aid devices even if conventional amplification provides no added benefit over his/her acoustic hearing. Postoperatively, participants are tested in his/her preferred listening program (cochlear implant sound processor program) and in his/her everyday listening condition.

Speech stimuli may be delivered via an audiometer with a CD or MP3 player or by proprietary software developed by Advanced Bionics called ListPlayer.

Audiometric and speech perception testing at post device activation intervals is to be conducted prior to any device (i.e. cochlear implant sound processor, hearing aid, EAS sound processor) adjustment and/or optimization of program 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.

The study participant's commercial ear-level (i.e. Naída family) Advanced Bionics cochlear implant sound processor (which provides electric only stimulation) should be checked routinely and adjusted if necessary as done clinically at each scheduled test visit. Participants that qualify and are fit with an AB prototype EAS sound processor at the defined test interval outlined within the study protocol (EAS fitting visit); will use and be tested wearing this device for the remaining scheduled postoperative test intervals that are outlined accordingly within the investigational plan. Should the participant's residual acoustic hearing in the implanted (treated) ear decrease to a level outside the EAS fitting inclusion criteria during the 12 month test interval, he/she should resume use of his/her commercial (owned) Advanced Bionics cochlear implant sound processor and the AB EAS device be returned to his/her managing hearing care center.

In the event that study participants qualifying and using the EAS sound processor device experiences any issue (i.e. requires replacement and/or exchange) during the clinical study; the participant should resume use of his/her owned cochlear implant sound processor device so that the participant is never without sound until a replacement EAS device is received from Advanced Bionics. Should the participant experience an issue with the EAS study device in and/or around a scheduled study test visit; the test interval should be rescheduled within a two-week period from the originally scheduled date to allow time for a replacement EAS device to be sent to the participant. This is recommended in an effort to maintain consistency in study testing at scheduled intervals with study participants.

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.

AzBio Sentence Test

The AzBio Sentence Test (Spahr and Dorman, 2005) is a validated test of open-set sentence recognition ability. The test will be administered in noise (target and noise 0° azimuth) at 60 dBA + 5 dB SNR using Speech-spectrum Noise (SSN) and scored as total number of words correct which will be expressed for results/reporting as percentage correct. The sentence tokens include both male and female speakers.

8.3.3 Patient Questionnaire:

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.

Abbreviated Profile of Hearing Aid Benefit (APHAB)

The APHAB (Cox and Alexander, 1995) will be used as a subjective, self-reported assessment of hearing status and hearing capability in everyday life. The questionnaire will be administered pre and post-treatment to participants. APHAB is designed to measure self-reported auditory / communicative disability in various everyday situations. There are four subscales that are evaluated within the APHAB questionnaire: Ease of Communication (EC) the strain of communicating under relatively favorable conditions; Reverberation (RV) Communication in reverberant rooms such as classrooms; Background Noise (BN) communication in settings with high background noise levels and Aversiveness (AV) the unpleasantness of environmental sounds.

8.3.4 Additional Test Measures:

Sponsor-developed patient questionnaires apart from the SSQ and APHAB listed above may be used with study participants at different points throughout the study. Questionnaires and/or patient report scales related to Speech, Music Perception, Sound Quality or Device Usability, for example, may be additionally administered to participants during the feasibility study at various test intervals. Sponsor developed questionnaires and/or feedback may be obtained from the participating study centers related to hardware, software, programmability or device usability during the study.

8.3.5 Summary: Speech perception testing procedures

Table 1 summarizes the speech testing that will be conducted at study test intervals. Each interval is described in further detail below. (Study Visits section 9.0).

Table 1. *General summary of speech perception testing.*

	Soundfield Test Condition		
Test	Preimplant Baseline Evaluation (Newly Implanted Group) (hearing aids)	Postimplant Evaluations through 12 Months Post Initial Device Fitting Visit (Newly Implanted and Existing Implanted Groups) (Implant; Implant+Acoustic hearing)	Postimplant Evaluations during EAS Extended Use Arm (Newly Implanted and Existing Implanted Groups) (Implant)
CNC words (60 dBA)	Unilateral aided right ear* Unilateral aided left ear*	Treated ear*	N/A
AzBio sentences in noise (60 dBA + 5 dB SNR; SSN)	• Unilateral aided ear to be implanted* • Bilateral listening condition**	Treated ear * Bilateral listening condition**	Treated ear *

*Plug and Muff method to be used in the ear contralateral to the one being measured for all speech perception testing

**Bilateral listening condition refers to a participant's everyday listening condition (with both ears). Postoperatively: may be one of the following conditions: cochlear implant alone in one ear + acoustic hearing (with or without amplification) in opposite ear; combined electric+acoustic (EAS) hearing in implanted ear + acoustic hearing (with or without amplification) in opposite ear

9.0 Study Visits

9.1 Newly Implanted Group: Pre-and postoperative visits are scheduled and occur at the study site (see Table 2 for summary of study visits)

Baseline Visit

Baseline information consists of collection of participant demographics, pertinent medical history, hearing and amplification history (i.e. etiology and onset of hearing loss, date of birth, gender, duration of hearing loss, amplification use). Note: 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 hearing aid trial. If determined by the investigator that a potential study participant has not received an appropriate and/or adequate trial and/or has never trialed conventional amplification devices, a 2-week hearing aid trial period would need to be completed prior to baseline test measures.

The following test measures are administered at the Baseline Visit:

Audiometric Testing:

- Tympanometry, each ear

- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear

- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

  Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; ear to be implanted *(Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Note: Clinician will need to confirm the participant's response to any pure-tone stimulus presented at 125 and 250 Hz as auditory "heard" versus vibrotactile "felt" and record these responses accordingly

Speech Perception Testing:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in each of the following conditions:
  - Unilateral Aided Right Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
  - Unilateral Aided Left Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided, Ear to be Implanted (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ Questionnaire – Standard Version)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form

Surgery

During surgery, participants will be implanted unilaterally with the commercially available HiRes 90K™ Advantage implant with HiFocus™ Mid-Scala electrode. The HiFocus™ Mid-Scala electrode lends itself to either a small cochleostomy or round window surgical approach (approach determined by implanting surgeon based on preference and experience and patient's cochlear anatomy). The HiFocus™ Mid-Scala can be inserted with or without a disposable tool. Although the HiFocus™ Mid-Scala does not require an insertion tool, an optional disposable tool is provided. Postoperative stay at hospital is determined by the participant's recovery with the implanting surgeon's recommendation.

A surgical questionnaire will be completed by the implanting surgeon at the time of the implant procedure.

Note: Implant surgery to be completed within 12 weeks of the Baseline Visit. If the surgery date exceeds this time frame, Baseline measures including tympanometry, audiometric and speech perception testing will need to be re-evaluated.

Postoperative Initial Device Fitting

Device activation at the participating study site will occur *within 3-6 weeks* following implantation. The following procedures will be completed at the initial activation visit:

Audiometric Testing:

- Tympanometry, each ear
- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear

Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Initial Device Fitting:

The participant is fit and programmed with his/her commercial ear-level (i.e. Naída family) AB cochlear implant sound processor (ordered as part of the participant's Bionic Ear System) for the treated ear. Method of fitting (software and coding strategy) will be completed using the commercially available programming software, SoundWave™ Professional Suite and the Clinicians Programming Interface (CPI). Rate and parameter settings will be selected by the managing clinician.

Note: Participant maintains and continues his/her *everyday* acoustic hearing condition for the non-implanted ear.

Using the participant's AB commercial sound processor (owned), please test the following audiometric condition:

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear *(Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Postoperative Follow-Up Visits

1 Week Post Initial Device Fitting Visit: *Visit should be scheduled within 7-10 days from the activation visit date*

Audiometric Testing:

- Tympanometry, each ear

- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear

- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Note: Participants with documented measurable functional postoperative hearing meeting study inclusion criteria for EAS Fitting as defined by unaided low frequency audiometric hearing thresholds in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz, are identified to the Study Sponsor. Audiometric threshold testing is repeated at the 1 month post device activation visit to reconfirm unaided low frequency hearing sensitivity and stability of thresholds to proceed with EAS device fitting accordingly.

Device Re-Programming (if necessary)

- Adjustment/optimization of participant's commercial device parameters as needed or recommended by managing clinician.

1 Month Post Initial Device Fitting Visit: *Visit should be scheduled within 4 weeks (+/- 7 days) from the activation visit date*

Audiometric Testing:

- Tympanometry, each ear

- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear

- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Using the participant's AB commercial sound processor (owned), please test the following audiometric condition:

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:

Note: The participant's Preferred Listening Program for his/her AB commercial sound processor is to be used during speech perception test measures:

- CNC Word Test (Quiet) – (Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:

- Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

- Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ-B Questionnaire)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form

Device Re-Programming (if necessary)

- Adjustment/optimization of participant's commercial device parameters as recommended by managing clinician. Participant's target program is achieved by this study interval.

Note: Participants with documented measurable functional postoperative hearing, as defined by unaided low frequency audiometric hearing thresholds in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz will be fit with the EAS device at this visit **following completion of the above audiometric, speech perception and questionnaire measures with the patient's commercial cochlear implant sound processor.*

TESTING FOR THE 1 MONTH INTERVAL IS COMPLETE AT THIS POINT FOR PARTICIPANTS THAT DO NOT MEET THE EAS DEVICE FITTING INCLUSION CRITERIA.

Prototype Electric Acoustic Stimulation (EAS) Device Initial Fitting/Programming:
Participants meeting the defined inclusion criteria will be fit with a prototype Advanced Bionics (AB) Cochlear Implant Sound Processor and EAS Earhook and programmed using an investigational version of SoundWave™ programming software and Clinicians Programming Interface (CPI). The prototype sound processor and EAS earhook is designed to deliver a combined electric plus acoustic stimulation (EAS) in one device. The prototype EAS sound processor is similar to the participant's commercial ear-level (i.e. Naída family) Advanced Bionics cochlear implant sound processor with the added capability and parameter settings for this combined EAS sound delivery. Participants may be provided with programs intended to stimulate the cochlear implant only or the combined electric-acoustic sound delivery. *At scheduled study intervals, the participant's preferred EAS program (combined electric-acoustic stimulation) should be used during testing.* Rate and parameter settings will be selected by the managing clinician. Participants will be encouraged to use the EAS device during all waking hours of all daily activities that are currently anticipated uses of commercially approved sound processors. For water activity, participants will be encouraged to remove the EAS device. An alternative would be for the participant to use his/her owned commercial device and place in an Advanced Bionics waterproof enclosure, AquaCase ([redacted], when using for water activities.

Using the AB <u>prototype EAS sound processor</u>, please test the following speech perception measures/conditions:

Speech Perception Testing:

Note: The participant's Preferred Listening Program for the EAS sound processor is to be used during speech perception test measures:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following condition:
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Sponsor developed Usability Questionnaire

Important Notation regarding Scheduling of Postoperative Visits

All newly implanted study participants, irrespective of meeting the inclusion criteria for EAS device fitting, will be scheduled following the one month post initial fitting visit for 3, 6 and 12 month study test intervals at the respective study site. These postoperative visit time windows are projected based on the participant's initial device activation date (+/- 14 days).

2 Months Post Initial Device Fitting Visit (1 Month Post EAS device fitting): *Visit should be scheduled within 4 weeks from the 1 month initial device fitting visit (+/- 7 days)*

NOTE: THIS VISIT IS SCHEDULED FOR PARTICIPANTS THAT HAVE BEEN FIT WITH THE EAS SOUND PROCESSOR DEVICE. PARTICIPANTS NOT MEETING THE EAS INCLUSION FITTING CRITERIA ARE NOT SCHEDULED FOR THIS VISIT AND RETURN FOR THE 3, 6 AND 12 MONTH POSTIMPLANT TEST INTERVALS.

Audiometric Testing:

- Tympanometry, each ear

- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear

- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Using the AB prototype EAS sound processor, please test the following audiometric condition:

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:

Note: The participant's Preferred Listening Program for the EAS sound processor is to be used during speech perception test measures:

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following condition:
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ-B Questionnaire)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form
- Sponsor developed Usability Questionnaire

Device Re-Programming (if necessary)

- Adjustment/optimization of participant's AB commercial device parameters and/or EAS prototype program parameters as recommended by managing clinician. Participant's EAS target program is achieved by this study interval.

3, 6 and 12 Months Post Initial Device Fitting: *Visits should be scheduled within 12, 24 and 48 weeks respectively from the initial device fitting date (+/-14 days)*

Audiometric Testing:

- Tympanometry, each ear
- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear
- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Note: If the study participant was fit with an AB prototype EAS sound processor, and continues to meet the functional residual hearing criteria (defined as unaided low frequency audiometric hearing thresholds in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz), he/she should be tested for all aided measures at this study visit using the EAS device.

If the participant was not fit with an AB prototype EAS sound processor (outside EAS fitting inclusion criteria), he/she should be tested using his/her AB commercial (owned) sound processor for all aided test measures at this interval.

If no preserved functional residual acoustic hearing has been previously documented and/or if the participant loses functional residual hearing as defined in the inclusion criteria, the participant should resume use and be tested with his/her AB commercial (owned) cochlear implant sound processor for these study intervals. <u>The investigational EAS device should be returned expeditiously to the managing study site should functional residual hearing be lost.</u>

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:
Note: The participant's Preferred Listening Program is to be used during speech perception test measures. Participants fit with the AB prototype EAS sound processor should use his/her preferred EAS program; participants <u>not fit</u> with the EAS device should use his/her AB commercial device and preferred CI listening program.

  - CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
    - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

  - Bilateral Condition

Self-Assessment Questionnaire(s):
- Speech, Spatial and Sound Qualities (SSQ-B* / Standard Version Questionnaire)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form
- Sponsor developed Usability Questionnaire

**Note: The SSQ-B is administered at the 3 and 6 month test intervals; standard version administration at the 12 month test interval visit.*

Device Re-Programming (if necessary)
Adjustment/optimization of participant's AB commercial and/or prototype EAS device program parameters as needed or recommended by managing clinician.

<u>EAS Extended Use Arm - Optional</u>

Each participant completing the 12 Months Post Initial Device Fitting Visit will have the option to enroll in the EAS Extended Use Arm with annual follow-up. Enrollment is optional and subject to the willingness of the participant and the discretion of the managing clinician. The EAS Extended Use Arm, with annual follow-up, shall continue up until the point of full commercialization of EAS.

EAS Extended Use Arm - Annual Follow-up Visits:

24, 36, 48, etc. Months Post Initial Device Fitting (using EAS device): *Visits should be scheduled within 96, 144 and 192, etc. weeks, respectively, from initial device fitting (+/-8 weeks)*

Audiometric Testing:

- Unaided low-frequency air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000 Hz; unilateral, treated ear

Speech Perception Testing:

Note: The participant's Preferred EAS Listening Program is to be used during speech perception test measures:

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here*)

Self-Assessment Questionnaire(s):

- Sponsor developed Usability Questionnaires

Device Re-Programming (if necessary)

Adjustment/optimization of participant's prototype EAS device program parameters as needed or recommended by managing clinician.

EAS Extended Use Arm - Termination Visit:

Upon commercialization, each participant will have 12 weeks to return the investigational EAS device and to complete a Termination Visit unless the most recent follow-up visit occurred within a 12 week window prior to full commercialization.

Additionally, if a participant or clinician elects to cease use of the EAS device prior to commercialization, the Termination Visit shall be conducted if more than 12 weeks have elapsed since an Annual Follow-up Visit. In this case the clinician shall communicate with the subject to determine the reason for the cease of use of the EAS device.

Audiometric Testing:

- Unaided low frequency air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000 Hz; unilateral, treated ear

Speech Perception Testing:

Note: The participant's Preferred EAS Listening Program is to be used during speech perception test measures:

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here*)

Self-Assessment Questionnaire(s):

- Sponsor developed Usability Questionnaires

Table 2: Newly Implanted Group: Summary of Study Visit

Visit	Procedure
12 Month Test Interval - Required	
Baseline	• Eligibility, consent, and enrollment • Case History/Demographics (audiologic/otologic and medical) • Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; ear to be implanted • Speech perception testing: Monosyllabic words in quiet – unilateral aided each ear. Sentence Recognition in Noise – unilateral aided ear to be implanted and bilateral listening conditions • SSQ Standard, APHAB, and Sponsor developed Patient Report Form Questionnaires
Surgery *(within 12 weeks of Baseline)*	• Device placement. • Surgical Questionnaire completion.
Initial Device Fitting (within 3 to 6 weeks after surgery)	• Device programming with AB commercial external CI sound processor and SoundWave™ Professional Suite programming software • Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; treated ear
1 Week (within 7-10 days) Post Initial Device Fitting	• Unaided audiometric testing and Tympanometry measures; each ear • Device adjustment / optimization of program parameters if needed
1 Month Post Initial Device Fitting Date (within 4 weeks (+/- 7 days) of the initial device fitting date)	• Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; treated ear • Speech perception testing using participant's AB commercial sound processor: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – treated ear and bilateral listening conditions • Device adjustment / optimization of program parameters if needed • SSQ-B, APHAB and Sponsor developed Patient Report Form Questionnaires

	• AB prototype EAS sound processor initial fitting (if functional residual hearing criteria met) • Speech perception testing using EAS sound processor: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – bilateral listening condition • Sponsor developed Usability Questionnaire
2 Month Post Initial Device Fitting Date (1 month post EAS device fitting if criteria met for EAS). Visit to occur within 4 weeks from the 1 month post initial device fitting visit +/- 7 days.	• Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; treated ear • Speech perception testing: Sentence Recognition in Noise – bilateral listening condition only • Device adjustment / optimization of program parameters if needed • SSQ-B, APHAB, Sponsor developed Patient Report Form and Usability Questionnaires
3, 6 and 12* month post initial device fitting (visits are projected out (i.e. 12, 24 and 48 weeks respectively) based on the initial device fitting date +/- 14 days) **Study endpoint*	• Unaided audiometric testing and Tympanometry; each ear • Aided audiometric testing; treated ear • Speech perception testing: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – treated ear; bilateral listening condition • Device adjustment / optimization of program parameters if needed to participant's commercial device and/or EAS device • SSQ-B (3 & 6 Month), SSQ-Standard (12 Month), APHAB, Sponsor developed Patient Report Form and Usability Questionnaires
EAS Extended Use Arm – Optional	
Annual Follow-up Visits 24, 36, 48, etc. month post initial device fitting (visits are projected out (i.e. 96, 144 and 192, etc. weeks respectively) based on the initial device fitting date +/-8 weeks)	• Low frequency unaided audiometric testing; unilateral, treated ear • Speech perception testing: Sentence Recognition in Noise – treated ear • Device adjustment / optimization of program parameters if needed to participant's EAS device • Sponsor developed Usability Questionnaires
Termination Visit	• Low frequency unaided audiometric testing; unilateral, treated ear • Speech perception testing: Sentence Recognition in Noise – treated ear • Sponsor developed Usability Questionnaires

9.2 Existing Implanted Group: Study Visits are scheduled and occur at the study site (see Table 3 for summary of study visits)

Existing implanted recipients with a HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode fit with a commercial ear-level sound processor (i.e. Naída family) meeting inclusion criteria for the EAS Fitting (functional preserved acoustic low frequency hearing in the treated ear up to 80 dB HL for at least one frequency from 125 – 1000 Hz) will be consented and scheduled for an initial fitting and follow-up study visits at the participants respective study site. The study visits are as follows:

Initial Visit (Baseline Assessment):

Baseline information consists of collection of participant demographics, hearing and pertinent medical history (i.e. etiology and onset of hearing loss, date of birth, gender, duration of hearing loss, amplification use) and the following test measures:

Audiometric Testing:

- Tympanometry; each ear
- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear
- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Using the participant's AB commercial sound processor (owned), please test the following audiometric condition:

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:
Using the participant's AB commercial sound processor (owned) and Preferred Listening Program, please test the following speech perception measures/conditions:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – *Treated Ear*: (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
  - Unilateral Aided or Unaided – *Non-implanted Ear:* (*Note: Participant should be tested in his/her everyday listening condition for the non-implanted ear which may be aided with amplification or unaided. Plug and muff method will be used in the ear contralateral to the one being measured here)*
- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech

spectrum noise (Target/Noise 0° Azimuth) in the following conditions:

- Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
- Bilateral Listening Condition

Prototype Electric Acoustic Stimulation (EAS) Device Initial Fitting/Programming:
Participants will be fit with a prototype Advanced Bionics (AB) Cochlear Implant Sound Processor and EAS Earhook and programmed using an investigational version of SoundWave™ programming software and Clinician's Programming Interface. The AB prototype sound processor and EAS earhook is designed to deliver a combined electric plus acoustic stimulation (EAS) in one device. The prototype sound processor is similar to the participant's commercial ear-level (i.e. Naída family) Advanced Bionics cochlear implant sound processor with the added capability and parameter settings for this combined EAS sound delivery. Participants may be provided with programs intended to stimulate the cochlear implant only or the combined electric-acoustic sound delivery. *At scheduled study intervals, the participant's preferred EAS listening program (combined electric-acoustic stimulation) should be used during testing.* Rate and parameter settings will be selected by the managing clinician. Participants will be encouraged to use the EAS device during all waking hours of all daily activities that are currently anticipated uses of approved sound processors. For water activity, participants will be encouraged to remove the EAS device. An alternative would be for the participant to use his/her owned commercial device and place in an Advanced Bionics waterproof enclosure, AquaCase, when using for water activities.

Speech Perception Testing:

Using the AB <u>prototype EAS sound processor and</u> Preferred EAS Listening Program, please test the following speech perception measures/conditions:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following condition:
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ Questionnaire – Standard Version)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form
- Sponsor developed Usability Questionnaire

Device Optimization-Re-Programming:
Adjustment/optimization of participant's AB commercial and/or prototype EAS device program parameters as needed or recommended by managing clinician.

1 Month Post EAS Device Fitting Visit: *(Visit should be scheduled within 4 weeks from the EAS device activation visit date)*

Audiometric Testing:

- Tympanometry; each ear
- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear
- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

Using the AB prototype EAS sound processor, please test the following audiometric condition:

- Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:

Using the AB prototype EAS sound processor and Preferred EAS Listening Program, please test the following speech perception measures/conditions:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ-B Questionnaire)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form
- Sponsor developed Usability Questionnaire

Device Re-Programming (if necessary)

Adjustment/optimization of participant's AB commercial and/or prototype EAS device parameters as needed or recommended by managing clinician. Participant's target program with the EAS device is achieved by this study interval.

3, 6 and 12 Month Post EAS Device Fitting Visits (using EAS device): *(Visits should be scheduled within 12, 24 and 48 weeks (+/- 14 days) respectively from the EAS device activation visit date)*

Audiometric Testing:

- Tympanometry; each ear
- Unaided air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz; unilateral, each ear
- Unaided bone-conduction hearing thresholds at 250, 500, 1000, 2000, 3000 and 4000 Hz; unilateral, each ear

The study participant should be tested for all aided measures at this study visit using the EAS device.

Note: If an existing implanted participant loses functional residual hearing during the study (outside the EAS fitting inclusion criteria), the prototype EAS device should be removed and returned to the managing study center. The participant should resume use of his/her commercial (owned) cochlear implant sound processor. The study subject's participation in the feasibility will end at the respective test interval respectively.

Aided soundfield hearing thresholds at 250, 500, 750, 1000, 1500, 2000, 3000, 4000 and 6000 Hz; Treated ear *(Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*

Speech Perception Testing:
Using the AB <u>prototype EAS sound processor</u> and Preferred EAS Listening Program, please test the following speech perception measures/conditions:

- CNC Word Test (Quiet) – Two Lists of 50 words presented at 60 dBA (Target 0° Azimuth) in the following condition:
  - Unilateral Aided – Treated Ear *(Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear *(Note: Plug and muff method will be used in the ear contralateral to the one being measured here)*
  - Bilateral Listening Condition

Self-Assessment Questionnaire(s):

- Speech, Spatial and Sound Qualities (SSQ-B* / Standard Questionnaire)
- Abbreviated Profile of Hearing Aid Benefit (APHAB)
- Sponsor developed Patient Report Form
- Sponsor developed Usability Questionnaire

**Note: The SSQ-B is administered at the 3 and 6 month test intervals; standard version administration at the 12 month test interval visit.*

Device Optimization-Re-Programming:
Adjustment/optimization of participant's AB commercial and/or prototype EAS device program parameters as needed or recommended by managing clinician.

EAS Extended Use Arm - Annual Follow-up Visits:
Each participant completing the 12 Month EAS Device Fitting Visit will have the option to enroll in the EAS Extended Use Arm with annual follow-up. Enrollment is optional and subject to the willingness of the participant and the discretion of the managing clinician. The EAS Extended Use Arm, with annual follow-up, shall continue up until the point of full commercialization of EAS.

24, 36, 48, etc. Months Post Initial Device Fitting (using EAS device): *Visits should be scheduled within 96, 144, and 192, etc. Weeks, respectively, from the EAS device activation visit date (+/-8 weeks)*

Audiometric Testing:

- Unaided low frequency air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000 Hz; unilateral, treated ear

Speech Perception Testing:

Note: The participant's Preferred EAS Listening Program is to be used during speech perception test measures:

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here*)

Self-Assessment Questionnaire(s):

- Sponsor developed Usability Questionnaires

Device Re-Programming (if necessary)
Adjustment/optimization of participant's prototype EAS device program parameters as needed or recommended by managing clinician.

EAS Extended Use - Termination Visit
Upon commercialization, each participant will have 12 weeks to return the investigational EAS device and to complete a Termination Visit unless the most recent follow-up visit occurred within a 12 week window prior to full commercialization.

Additionally, if a participant or clinician elects to cease use of the investigational EAS device prior to commercialization, the Termination Visit shall be conducted if more than 12 weeks have elapsed since an Annual Follow-up Visit. If the Termination Visit is not required, the clinician shall communicate with the subject to determine the reason for the cease of use of the EAS device.

Audiometric Testing:

- Unaided low frequency air-conduction thresholds using insert earphones at 125, 250, 500, 750, 1000 Hz; unilateral, treated ear

Speech Perception Testing:

Note: The participant's Preferred EAS Listening Program is to be used during speech perception test measures:

- AzBio Sentence Test (Noise) – Two lists at 60 dBA with a +5dB SNR using speech spectrum noise (Target/Noise 0° Azimuth) in the following conditions:
  - Unilateral Aided – Treated Ear (*Note: Plug and muff method will be used in the ear contralateral to the one being measured here*)

Self-Assessment Questionnaire(s):

- Sponsor developed Usability Questionnaires

Table 3. Existing Implanted Group: Summary of study visits and procedures.

Visit	Procedure
12 Month Test Interval - Required	
Initial Visit (Baseline Assessment) and EAS Device Fitting	• Eligibility, consent, and enrollment • Case History/Demographics (audiologic/otologic and medical) • Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; treated ear • Speech perception testing using participant's ear-level commercial (owned) CI sound processor: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – treated ear and bilateral listening conditions • AB prototype EAS sound processor initial fitting if functional hearing criteria met • Speech perception testing using EAS sound processor: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – bilateral listening condition • SSQ Standard, APHAB, Sponsor developed Patient Report Form and Usability Questionnaires
1 Month Post EAS Device Fitting (within 4 weeks (+/- 7 days) of the EAS device fitting date)	• Unaided audiometric testing and Tympanometry measures; each ear • Aided audiometric testing; treated ear • Speech perception testing using EAS sound processor: Monosyllabic words in quiet –

	treated ear. Sentence Recognition in Noise – treated ear and bilateral listening conditions • Device adjustment / optimization of program parameters if needed • SSQ-B, APHAB and Sponsor developed Patient Report Form and Usability Questionnaires
3, 6 and 12* month post EAS device fitting (visits are projected out (i.e. 12, 24, 48 weeks) based on the EAS device activation date +/- 14 days) **Study endpoint*	• Unaided audiometric testing and Tympanometry; each ear • Aided audiometric testing; treated ear • Speech perception testing: Monosyllabic words in quiet – treated ear. Sentence Recognition in Noise – treated ear; bilateral listening condition • Device adjustment/optimization of program parameters if needed to participant's commercial device and/or EAS device • SSQ-B (3 & 6 Month), SSQ-Standard (12 Month), APHAB, Sponsor developed Patient Report Form and Usability Questionnaires
EAS Extended Use Arm – Optional	
Annual Follow-up Visits 24, 36, 48, etc. month post EAS device fitting (visits are projected out (i.e. 96, 144 and 192 weeks, respectively) based on the EAS device activation date +/- 8 weeks)	• Low frequency unaided audiometric testing; unilateral, treated ear • Speech perception testing: Sentence Recognition in Noise – treated ear • Device adjustment / optimization of program parameters if needed to participant's EAS device • Sponsor developed Usability Questionnaires
Termination Visit	• Low Frequency unaided audiometric testing, unilateral, treated ear • Speech perception testing: Sentence Recognition in Noise – treated ear • Sponsor developed Usability Questionnaires

9.3 Unscheduled Visits

Unscheduled visits to the participant's managing implant center or physician may be made at any time for evaluation of possible adverse events or to address any questions or concerns expressed by the participant that cannot be managed adequately by telephone or e-mail communication. These visits are considered routine and standard of care.

9.4 Advanced Bionics Prototype Sound Processor Return and/or Retention

Study participants meeting the functional residual hearing in the implanted ear as defined within this study protocol, will retain use of the AB Prototype Sound Processor throughout the feasibility trial. Beyond the defined study endpoint (12 month test interval) participants (newly

implanted and existing implanted groups) fit with the AB Prototype Sound Processor have the option to retain the device until the time the AB commercial EAS device is released.

Newly implanted study participants not meeting the functional residual hearing criteria to be fit with the AB Prototype Sound Processor and/or who lose functional residual hearing post implant treatment (and fall outside the defined fitting criteria) during the 12 month test interval will return the prototype sound processor to Advanced Bionics. The participant maintains and/or resumes use of his/her AB commercial (owned) sound processor throughout the feasibility study and thereafter. Should existing group study participants lose acoustic residual hearing and fall outside the defined fitting criteria for the study during the 12 month test interval, the prototype EAS sound processor will be returned to Advanced Bionics.

10.0 Statistical Methods

General Considerations

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 50 total subjects is deemed sufficient for determining the feasibility for the development of electric and acoustic stimulation technology.

11.0 Efficacy Measures

An objective of the feasibility study is to facilitate and complete development of a combined input acoustic and electric stimulation (sound delivery) technology. 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. Postimplant audiometric hearing thresholds will be compared to preimplant thresholds in the newly implanted group to assess preservation of any low frequency acoustic residual hearing in the treated ear post intervention with the HiRes 90K™ Advantage cochlear implant with the HiFocus™ Mid-Scala electrode. Specifically, unaided pure tone hearing threshold measurement in the treated ear compared to preimplant audiometric thresholds (using a pure-tone average of .125, .25, .5 and 1 kHz for comparison) will be assessed. Individual and group comparisons will be made. Results will be tabulated and summarized based on pre- to postoperative change in pure-tone average (PTA).

2. Additionally, monosyllabic word recognition performance in quiet for the treated ear using the CNC word test and sentence recognition in noise using AzBio sentence test pre-to-post device activation will be compared, tabulated and summarized for the newly

implanted group. AzBio sentence understanding in noise pre-to-postoperatively will also be compared, tabulated and summarized in the bilateral listening condition. The intent of this individual and group comparison is to address the contribution and benefit of the implant treatment option in a partial deafness population as compared to the preimplant listening condition.

3. The Speech, Spatial Qualities (SSQ) and the Abbreviated Profile of Hearing Aid Benefit (APHAB) questionnaire score comparison pre-to-post device activation will be conducted (in the newly implanted group) to provide a subjective measure of patient perceived hearing performance/auditory benefit with this combined technology. The SSQ and APHAB will aid in providing a measure of subjective perceived benefit; individual and group comparisons will be made. Additional subjective data collected (i.e. Sponsor developed questionnaires) in the feasibility study will also be tabulated and summarized to evaluate amount of improvement, no change or decrement.

4. Additional audiometric, speech perception measures in addition to Sponsor developed subjective questionnaires will also be assessed and evaluated for all study participants (i.e. newly implanted and existing implanted groups) post EAS device system fitting and over chronic use period of time (i.e. contralateral ear hearing threshold monitoring; subjective reporting).

12.0 Safety Measures

12.1 Adverse Event Reporting

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. The AEs will be recorded and tracked between the completion of the informed consent form and two weeks after the subject's last follow-up visit. During the EAS Extended Use Arm, reporting shall be limited to those AEs deemed device-related or procedure-related by the Investigator per the records requirements of 21 CFR 812.140(a)(3)(ii).

The following risks are identified as anticipated Adverse Events:

- Newly Implanted Group
    - Risks specific to this study
        - Possible loss of all residual hearing in the ear to be implanted, which may be permanent
            - Any Newly Implanted study participant experiencing a shift in audiometric threshold of 50 dB or greater at 2 or more test frequencies from 125-1000 Hz will be reported as an anticipated Serious Adverse Event under this feasibility study. Given the postoperative audiometric hearing threshold fluctuations expected after cochlear implantation (i.e. potential middle ear

fluid postop); the Serious Adverse Event reporting as defined will be reported at the 3 month postoperative test interval, a point at which things such as confounding middle ear involvement may resolve.

- Loss of all residual hearing may result in added difficulty hearing in various everyday listening situations. For example, locating the direction of a sound in the environment, perception of music may be altered or degraded, hearing your own voice or in the detection of sounds such as a door-knock or telephone ring.

- 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

- 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

- Newly Implanted and Existing Implanted Group Participants
  - Overall risks of being fit with and using prototype external sound processor systems are considered no greater than those associated with the commercial external sound processor system in general
  - Choking hazard due to small parts/pieces of the device
  - Residual natural hearing damage if programming error or sound overstimulation
  - Uncomfortable hearing sensation or overly-loud sound due to hardware malfunction
  - Irritation of skin with prototype device
  - Neural tissue damage due to chronic overstimulation
  - Device malfunction or explant due to exposure to high levels of static electricity and electric shock due to non-isolated conduction paths when connected to medical equipment
  - A risk of additional loss of residual acoustic low frequency hearing as a factor of chronological age (i.e. presbycusis) and/or etiology of the hearing loss may be experienced

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 CRF (see Exhibit 2, Attachment 2.3, Appendix B for all CRFs) during the 12 month test interval. During the EAS Extended Use Arm, AEs deemed device-related or procedure-related by the Investigator will be recorded on the Adverse Event CRF. Information to be recorded on the CRF should include, but is not limited to:

- Date that event was first detected
- Description of event, duration, and severity
- Course of action taken
- 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 notice 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.

12.2 Assessment – Feasibility Study

Objectives of this feasibility study are to obtain preliminary data regarding the safety of cochlear implantation in individuals with partial deafness and complete technology development for a combined input electric and acoustic sound delivery system. 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.

All adverse events (AE) 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. Adverse Events will be recorded at participating study sites on a provided electronic case report form and will include but are not limited to the following information:

- Date of onset of the AE
- Date reported to the managing center
- Description of the AE
- Seriousness
- Investigator's assessment of the relatedness of the AE to the procedure and/or device

- Treatment/Intervention
- Outcome

All AEs are to be reported to the FDA in accordance with the IDE regulation. Participating study sites will report to their Institutional Review Boards in accordance with study guidelines.

13.0 Risk Analysis

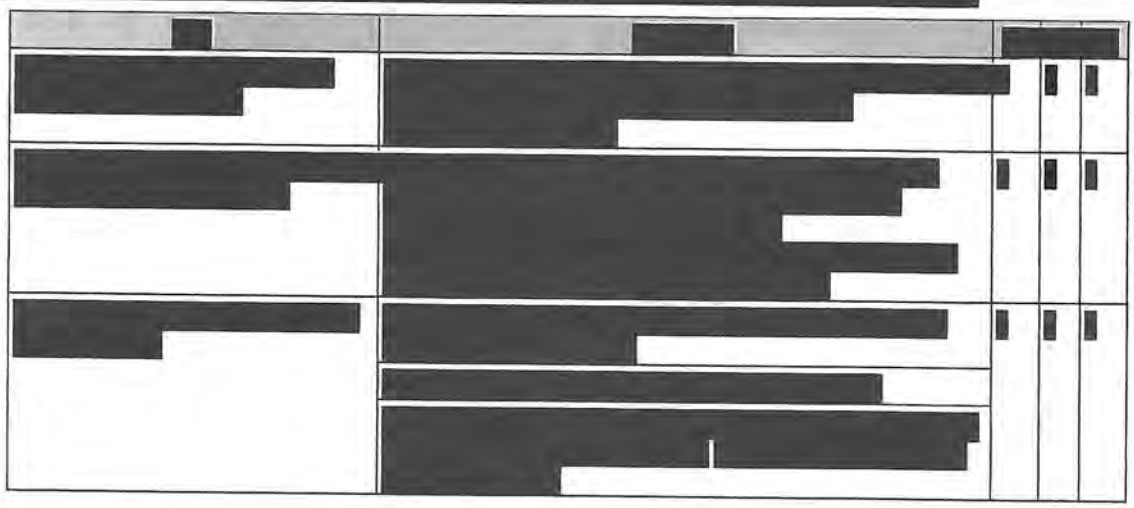
13.1 Approved Products:

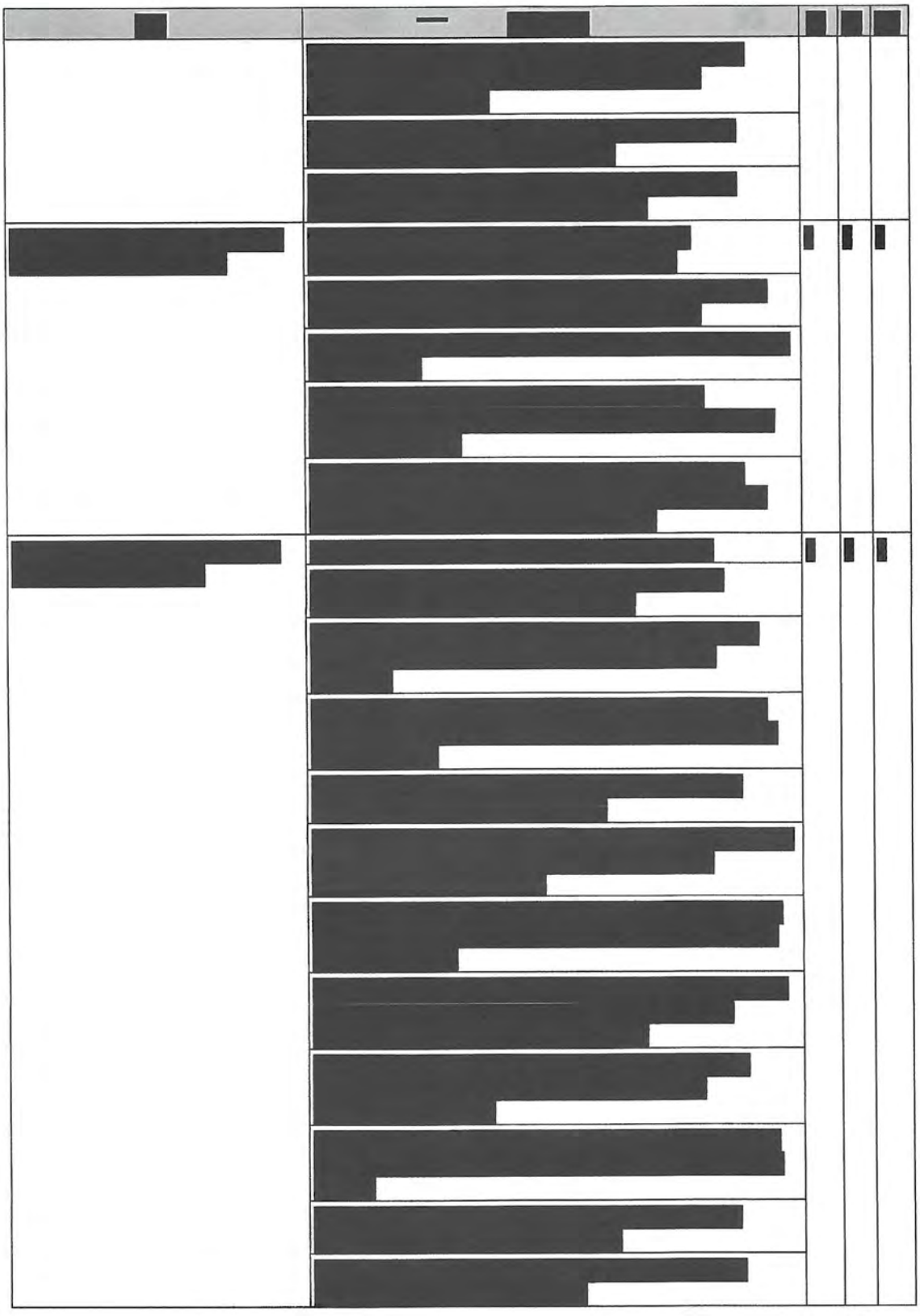
As the EAS system investigated in this study is based upon the existing approved HiResolution Bionic Ear System (HiRes 90K System) (P960058), the anticipated risks for the investigational system include those for the approved system. [redacted] The risks associated with use of the approved products are contained in those products' instructions for use. The risk analysis contains the determination that the benefit provided by these types of devices outweighs any residual risk.

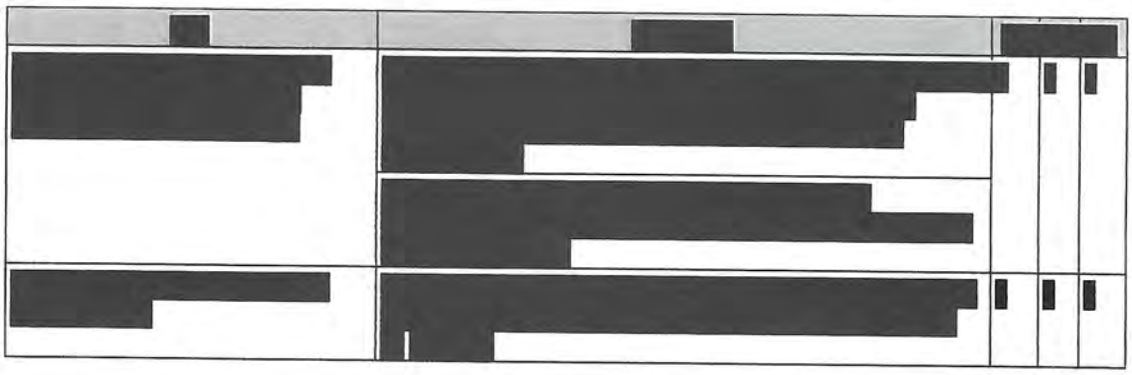
13.2 Investigational hardware risks:

The only foreseeable risks associated with investigational hardware that are not covered by the approved HiRes 90K System risk analysis are those that are associated with the manufacture of the investigational hardware and the application of acoustic stimulation. These risks are mitigated through combinations of safety and system testing, design inspections, and advisories provided to the patient.

Risks associated with investigational hardware in general are covered in the Risk Analysis Report for External Hardware Component Feasibility, [redacted]





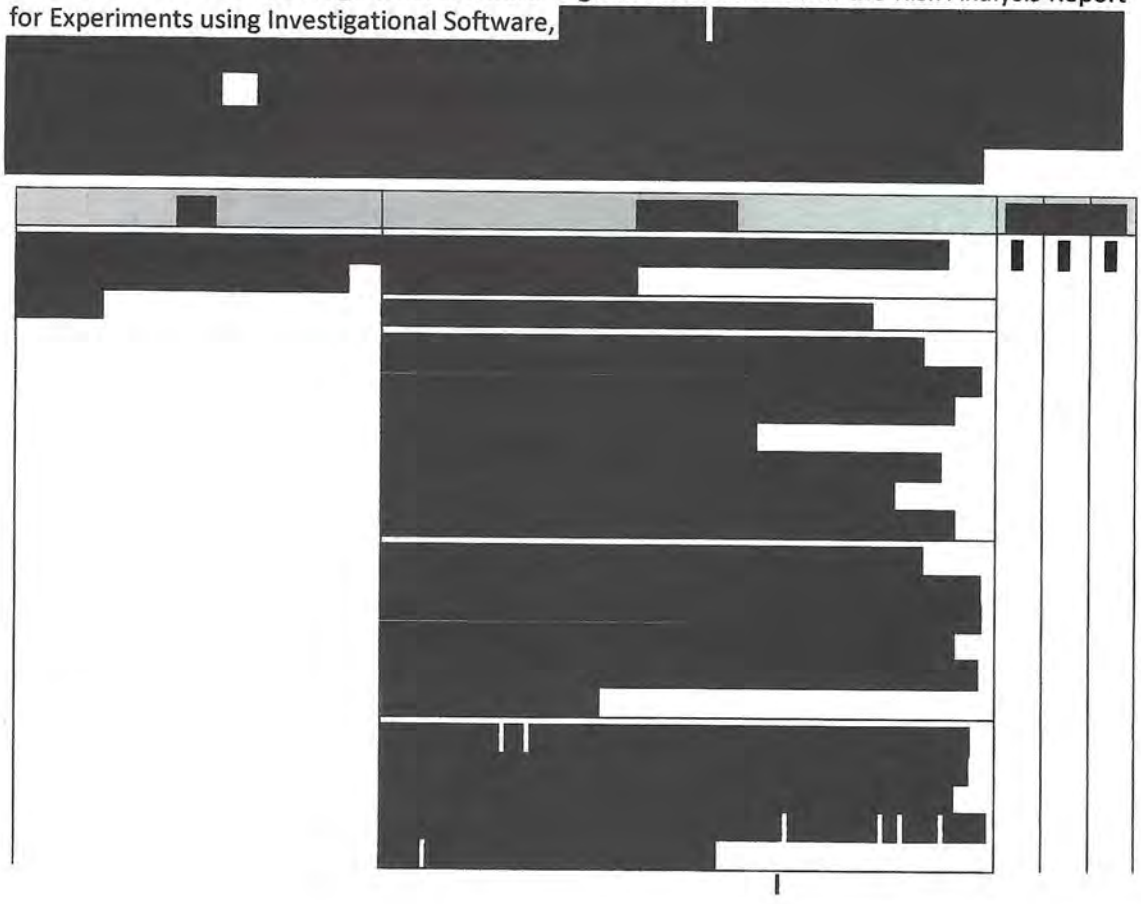


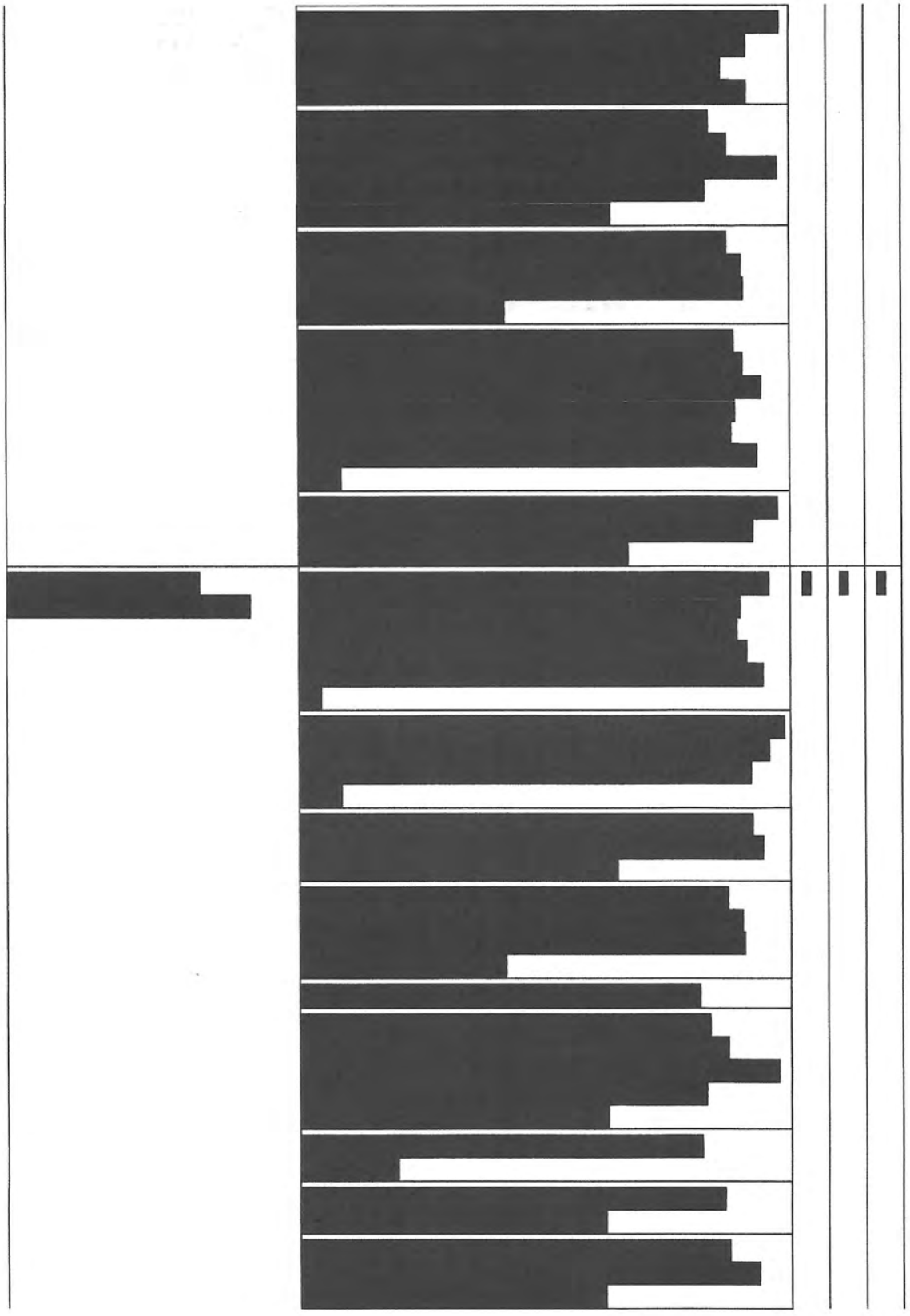
*This Investigational Plan serves as the Experimental Plan for the participating investigational sites.

13.3 Investigational software risks:

The only foreseeable risks associated with investigational software that are not covered by the approved HiRes 90K System risk analysis are those that are associated with programming errors during adaptation of existing strategies and the application of acoustic stimulation. These risks are mitigated through combinations of safety and system testing, and advisories provided to the patient.

Risks associated with investigational software in general are covered in the Risk Analysis Report for Experiments using Investigational Software,





[redacted]

13.4 Surgical and Device Risks:

Risks associated with the surgical procedure of the HiRes90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode are no greater than those associated with cochlear implantation in general. Use of the Advanced Bionics HiRes 90K™ Advantage cochlear implant with HiFocus™ Mid-Scala electrode does 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 for this feasibility study is adults with partial deafness presenting with more acoustic residual hearing than the currently approved patient population. Cochlear implantation in individuals in this population may potentially benefit from a combined sound input to the treated ear of acoustic hearing plus electrical stimulation. However the ability to preserve and the amount of residual low frequency hearing remains a relevant consideration with respect to functionality and outcomes. It is imperative to consider that even if residual acoustic hearing is lost (not preserved post cochlear implantation treatment), the electrode on its own can support a higher level of speech understanding than with the individual's natural or acoustic only pre-treatment condition. Thus, hearing benefits experienced by study recipients are anticipated to be significant, even if residual hearing is not preserved. 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 ≥2 weeks 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.

Overall risks of being fit with and using prototype external sound processor systems are considered no greater than those associated with your commercial external sound processor system in general. The only foreseeable risks associated with investigational hardware are those associated with the manufacture of the investigational hardware and software and the application of acoustic stimulation combined with the electric stimulation from your cochlear implant. These risks are lessened by combinations of safety and system testing, design inspections and advisories provided to you by the Sponsor. Potential risks associated with investigational hardware and software may include: choking hazard due to small parts/pieces of the device; residual natural hearing damage if programming error or sound overstimulation; uncomfortable hearing sensation or overly-loud sound due to hardware malfunction; irritation of skin with prototype device; neural tissue damage due to chronic overstimulation; device malfunction or explant due to exposure to high levels of static electricity and electric shock due to non-isolated conduction paths when connected to medical equipment. These circumstances are considered rare but nevertheless important to identify to you prior to your participation. As mentioned above, the Sponsor through combinations of safety and system testing, design inspections and precautions outlined to you when using the device has worked to ensure these types of risks are lessened. Your time spent participating is considered to be an inconvenience associated with study participation as well.

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 [redacted]

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 not 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 not contraindicated except under specific circumstances.

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.

13.5 Safety Testing of Investigational Devices

Prior to patient testing, the investigational device shall be subject to safety and functional testing as required to verify the mitigations identified in the risk analysis above. Approval of investigational devices for use by patients will be in accordance with the Advanced Bionics Quality System Requirements. Test results will be documented in safety and system test reports for each iteration of investigational hardware or software; these reports will be reviewed and approved according to Advanced Bionics' change control process.

The following table references the processes followed and reports generated to confirm safety of the investigational system. For all documents referenced in the table, please refer to Exhibit 1 of the original IDE application: [redacted]

Investigational Subsystem	Process Defined By	Risk Analysis Report	Patient Safety	Device Function
Hardware	[redacted] Conduction of Patient Experiments to Assess Design Feasibility of External Components	[redacted]	Hardware Safety Test Plan/Report	System Test Plan/Report
Software	[redacted] Conduction of Patient Experiments with BEPSnet, BEDCS, BEPS+ or Experimental SoundWave Software	[redacted]	Software Safety Test Plan/Report	

13.5.1 Stimulation Safety

Only FDA approved electrical stimulation strategies (CIS, MPS and SAS, HiRes, and HiRes with Fidelity 120, HiRes Optima) will be used. These approved strategies all conform to established parameters for stimulation safety. As the approved HiRes 90K cochlear implant is used in this evaluation, there are no new risks associated with the implant including the controls for electrical stimulation which remain unchanged.

Acoustic stimulation gains will be set by an audiologist based on traditional fitting formulae and standard clinical practice (e.g. DSL[i/o], NAL-RP). Additionally, a proprietary fitting formula under development will be assessed in comparison to standard fitting formulas. Investigators will

explore the relationship between acoustic and electric frequency representations. The external products undergoing feasibility evaluation will be tested to ensure that the following stimulation safety criteria are met:

- Sound pressure level output by the device does not exceed the maximum power output set by the clinician.
- Maximum power output will be subject to a limit of 120 dB SPL.

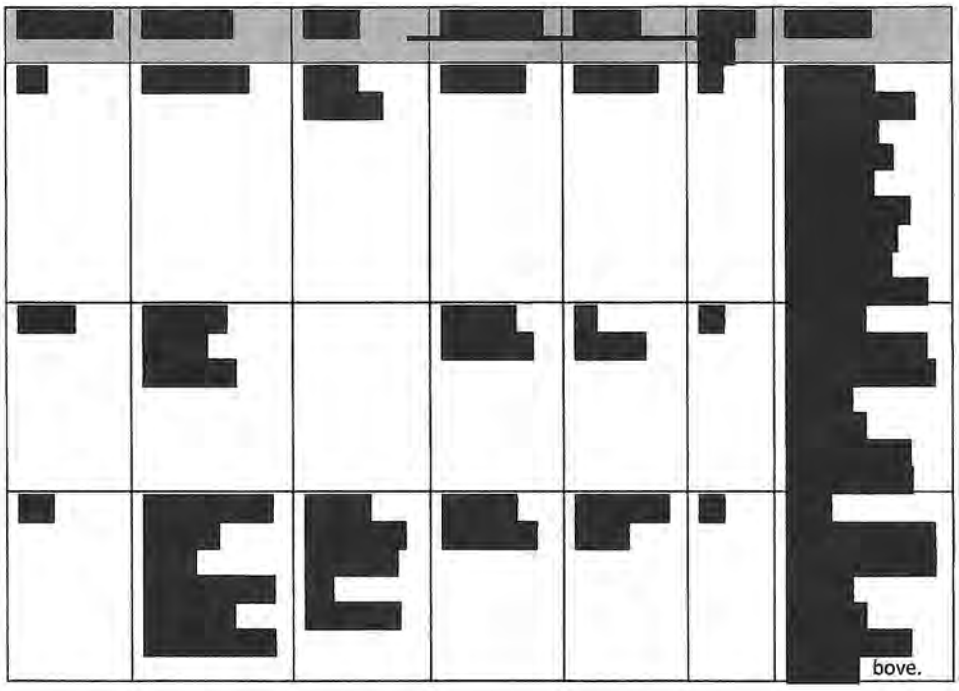
13.5.2 Software Controls

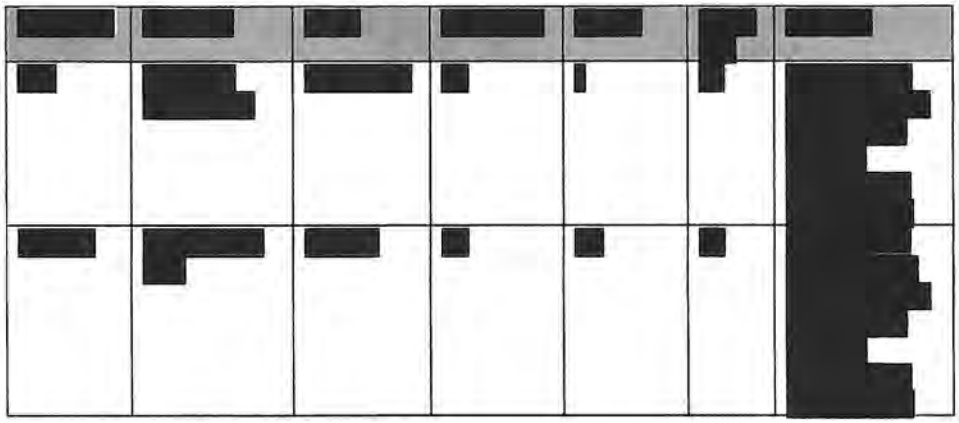
The fitting software that establishes the electrical stimulation parameters for the patient restricts the range of stimulation pulse widths and amplitudes, and assumes the electrode array with the smallest contact area is being used, so that charge density limits of 216 $\mu C/cm^2$ are never exceeded. The stimulation parameters in the resulting patient program conform to this charge density limit.

Similarly, the fitting software that establishes the acoustic gains restricts the maximum power output entered by the audiologist to no greater than 120 dB SPL.

The stimulation parameters associated with the patient's speech processor and strategy will be used as the starting point for the trial. The patient program might need to be modified based upon perceptual feedback from the patients. The limits that restrict stimulation amplitude, charge density and charge balance will not be modified or altered by the software. The specific elements of the patient programming software, associated ranges and the safety impact of making any changes is tabulated in Table 4 below.

[redacted] 4 – [redacted]





13.5.3 Biocompatibility

All new external mechanical packages will be subject to biocompatibility testing prior to their use with patients. The biocompatibility tests will assess for cytotoxicity, skin sensitization, and primary skin irritation as required. This requirement per ISO 10993-1 is needed when skin contact duration is greater than 30 days.

Table 5 references the safety test plans and safety test reports included in the IDE attachment and appendix materials for each of the experimental software platforms which will be used in the study. These platforms may include SoundWave EAS, BEDCS, BEPSnet and BEPS+. For all documents referenced in the table, please refer to Exhibit 1 of the IDE application.

Modification of the patient program to account for sound quality changes experienced by trial subjects will managed within the limits prescribed in Table 4 above.

Table 5: Relevant Safety Test Plans and Safety Test Reports included as Appendix Material

Experimental Software Platform	Safety Test Plan	Safety Test Report
SoundWave EAS	Safety Test Plan	Safety Test Report for SoundWave EAS Software
BEDCS	Safety Test Plan for BEDCS Software	Safety Test Report for BEDCS Software
BEPSnet	Safety Test Plan - BEPSnet - With novel sound coding strategies	Safety Test Report - BEPSnet - With novel sound coding strategies

BEPS+	Electrical Safety	[redacted] Safety Test Plan for BEPSPlus	[redacted] Safety Test Report for BEPSPlus
	System Design	[redacted] System Test Plan and Report for BEPS+	

*Appendices 1.7-1.13 were provided in the original IDE application.

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 and/or continuance 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 (Exhibit 2, Attachment 2.3, Appendix C). 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 provided deviation report form (CRF) and maintained 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 respective IRB.

15.0 Health Insurance Portability and Accountability Act (HIPAA)

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 at each site. The monitor will visit the Investigator and the study facility at periodic intervals in addition to maintaining ongoing telephone, e-mail and/or letter contact. The monitor will maintain up-to-date personal knowledge of the study through observation, review of study records and source documentation, and discussion of the study with the Investigator and study personnel. The 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 at a site. 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 must be provided to Advanced Bionics:

- A copy of the protocol signature page, which serves as the Investigator Agreement, signed and dated by the Principal Investigator and Sub-Investigator(s), if applicable
- 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 must be used to submit data to Advanced Bionics (Exhibit 2, Attachment 2.3, Appendix B). Each subject will be assigned a unique identifier at the time of enrollment, which will be used on all eCRFs. Investigator responsibilities include obtaining adequate case histories for the subjects while participating in the research covered under this protocol. The Investigator agrees to maintain accurate source documentation as part of these case histories.

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

Newly implanted study 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, EAS prototype sound processor, EAS Earhook, study laptop and investigational SoundWave™ software will be shipped with the following label: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use." Participants qualifying for EAS device fitting will be fit and programmed with a prototype AB cochlear implant Sound Processor and EAS Earhook and programmed using an investigational version of the SoundWave™ programming software and Clinician's Programming Interface (CPI) supporting the EAS device.

18.4 Record Retention

All study records (e.g., protocol, correspondence with Advanced Bionics and the IRB, IRB approvals, eCRFs, patient records, consent forms, reports) must be maintained by the Investigator until notified by Advanced Bionics and at least as long as local document retention regulations require. If an Investigator opts to discontinue participation in the study, all records will be transferred to a mutually agreed designee (i.e., another Investigator). This transfer is subject to Advanced Bionics' approval and will be documented in writing with copies sent to Advanced Bionics, LLC. 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 Advanced Bionics, the FDA or other regulatory authorities to access all study records. The Investigator will notify Advanced Bionics promptly of all audit requests from government or other regulatory agencies and will promptly forward a copy of all audit findings to Advanced Bionics.

19.0 Suspension and Termination

19.1 Criteria for Terminating the Study

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.

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:

- To sign and adhere to the protocol and the clinical trial agreement.
- 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 conduct the investigation in accordance with the study protocol, clinical trial agreement, all applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or the FDA.
- To supervise all testing of human subjects.
- To ensure that all subjects are properly consented in English
- 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. Specifically, all investigators and investigational sites will be monitored on a continuing basis through the course of the clinical study to oversee compliance with the regulatory and clinical aspects of the study. The Clinical Monitor will maintain current personal knowledge of the study through observation, review of study records and source documentation, and discussion of the study with the investigators and study site staff.

Clinical Monitors will be members of the Clinical Research, OR Support or Technical Services Departments of Advanced Bionics who have been trained on the study protocol, 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 protocol and procedures (technical information on use of the investigational product may be reviewed by members of the Research and Development, Marketing, or 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 on-site visits:

- Confirm that the facilities continue to be appropriate and that the study records are stored in a secure location
- Conduct review and collection of regulatory documents
- Review subject informed consent forms for completeness and accuracy
- Confirm that the study protocol is being followed and that any changes in the protocol have been reported to the IRB and Advanced Bionics, 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 to Advanced Bionics 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 to Advanced Bionics 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
- 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 protocol, 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

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

20.4 Management of Site Noncompliance

Observations of noncompliance with the signed agreement, the 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

Advanced Bionics and investigators maintain files with regulatory documents (study protocol, 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 and the site maintains copies of all 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. The report, or a follow-up letter summarizing the report, is sent to the site, including follow-up action items and corrective actions to resolve deficiencies, if appropriate, for inclusion in the regulatory binder. A copy of the monitoring report is maintained by Advanced Bionics.

21.0 References

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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 to each participating study site as well for Institutional Review Board submission and review.

23.0 Study Sites and Investigators

Participating Centers	
Center: Midwest Ear Institute/St. Luke's Health System **Name of PI:** Robert D. Cullen, MD 4320 Wornall Road Kansas City, MO 64111 **IRB:** Saint Luke's Hospital of Kansas City IRB 4401 Wornall Road Kansas City, MO 64111 (816) 932-2000 Diana Dark, MD, Chair	**Center:** Vanderbilt Bill Wilkerson Center **Name of PI:** David Haynes, MD 1211 Medical Center Drive Nashville, TN 37232 **IRB:** Vanderbilt University Office for Human Research Protections 1313 21st Ave., South, Suite 504 Nashville, TN 37232-4315 (615) 322-2918 Todd W. Rice, MD, MSc, Medical Director
Center: Tampa Bay Hearing and Balance Center **Name of PI:** Loren J Bartels, MD, FACS 5 Tampa General Circle, Suite 610 Harbourside Medical Tower Tampa, FL 33606 **IRB:** Western Institutional Review Board (WIRB) 1019 39th Avenue SE, Ste. 120 Puyallup, WA 98374 (360) 252-2500 R. Bert Wilkins, Executive IRB Chair	**Center:** Washington University **Name of PI:** Richard A. Chole, MD, PhD 660 S. Euclid, Campus Box 8115 St. Louis, MO 63110 **IRB:** Washington University Human Research Protection Office 600 South Euclid Avenue, Campus Box 8089 St. Louis, MO 63110 (314) 633-7400 Jonathan Green, MD, Executive Chair
Center: University of Texas Southwestern Medical Center **Name of PI:** Brandon Isaacson, MD 5323 Harry Hines Boulevard Dallas, TX 75390 **IRB:** University of Texas Southwestern Medical Center IRB 5323 Harry Hines Blvd Dallas, TX 75390 (214) 648-3060 David Karp, IRB Chairperson	**Center:** New York University Langone Medical Center **Name of PI:** J. Thomas Roland Jr., MD 550 First Avenue, Skirball 7Q Silverstein Elevators New York, NY 10016 **IRB:** Office of Science & Research Institutional Review Board 1 Park Avenue, 6th floor New York, NY 10016 (212) 263-4110 Elan Czeisler, CIP, Director of IRB Administration

Center: Mayo Clinic Rochester **Name of PI:** Colin L. W. Driscoll, MD 200 First Street SW Rochester, MN 55906 **IRB:** Mayo Clinic IRB Office For Human Research Protection 201 Building, Room 4-60 200 First Street SW Rochester, MN 55905 (507) 266-4000 William Tremaine, MD, Director, Mayo Clinic Office of Human Research Protection	**Center:** Austin Ear, Nose & Throat Clinic **Name of PI:** James Kemper, MD 5750 Balcones Dr., Ste. 200 Austin, TX 78731 **IRB:** Western Institutional Review Board (WIRB) 1019 39th Avenue SE, Ste. 120 Puyallup, WA 98374 (360) 252-2500 R. Bert Wilkins, Executive IRB Chair
Center: House Clinic **Name of PI:** William Luxford, MD 2100 W. Third Street Los Angeles, CA 90057 **IRB:** St. Vincent Medical Center Institutional Review Board 2131 West Third Street Los Angeles, CA 90057 David Winsor, MD, Research Integrity Officer/Board Chair	**Center:** Georgetown University Hospital **Name of PI:** Michael Hoa, MD Department of Otolaryngology-Head and Neck Surgery 3800 Reservoir Rd. NW 1st Floor Gorman Building Washington, DC 20007 **IRB:** Georgetown University Institutional Review Board Medical-Dental Building, SW 104 3900 Reservoir Road NW Washington, DC 20057
Center: Oklahoma Ear Institute **Name of PI:** Betty Tsai, MD 825 N.E. 10th St. Oklahoma City, OK 73104 **IRB:** University of Oklahoma Health Sciences Center Institutional Review Board Office of Human Research Participant Protection 1105 N. Stonewall Ave, Library Building, Room 176 Oklahoma City, OK 73117 Karen Beckman, MD, Chairperson	**Center:** University of Missouri **Name of PI:** Arnaldo Rivera, MD Mu-ENT, Hearing and Balance 525 N. Keene St. Suite 201 Columbia, MO 65201 **IRB:** University of Missouri Institutional Review Board 905 Hitt Street 190C Galena Hall, DC 074 Columbia, MO 65201 Michele Kennett, Director of Human Subjects Protections
Center: University of Kentucky Medical Center **Name of PI:** Matthew Bush, MD 740 S. Limestone St. B317 Kentucky Clinic Lexington, KY 40536 **IRB:** University of Kentucky Office of Research Integrity	**Center:** University of Southern California **Name of PI:** Elina Kari, MD USC Caruso Department of Otolaryngology – Head and Neck Surgery Keck USC School of Medicine 1450 San Pablo Street, Ste. 5100 Los Angeles, CA 90033

315 Kinkead Hall Lexington, KY 40506 Lisa Cassis, PhD, Interim Vice President for Research	**IRB:** USC Health Sciences Institutional Review Board General Hospital Ste. 4700 1200 North Street, Los Angeles, CA 90033 Darcy Spicer, MD, Chair