Evaluation of the Naída CI L90 sound processor programmed with Target CI v.1.6 Fitting Software in Adult Users of the HiResolution™ Bionic Ear System.

Investigational Plan CR0124
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[redacted]

1.0 Synopsis

Study Title	Evaluation of the Naída CI L90 sound processor programmed with Target CI v. 1.6 Fitting Software in Adult Users of the HiResolution™ Bionic Ear System.
Sponsor	Advanced Bionics, LLC
Investigational Device	An investigational Naída CI L90 Processor programmed using investigational Target CI v.1.6 Fitting Software
Study Design	Prospective within-subjects repeated-measures study
Number of subjects	18 bilateral adult users implanted with a HiResolution Bionic Ear System (HiRes 90K™, HiRes 90K ™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D and CII with HiFocus electrode).
Inclusion Criteria	• Ability to provide Informed Consent • 18 years of age or older • Bilateral users of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D and CII with HiFocus electrode) • Willingness to participate in all scheduled procedures outlined in the study investigational plan • Minimum of 6 months of CI experience for each ear • At least moderate open-set speech recognition abilities with implant in each individual implanted ear, as defined by achieving a score of ≥ 50% words correct in the AzBio Sentence Test in quiet using a Naída CI M90 research processor • English language proficiency, as determined by the investigator • Willingness to use a behind-the-ear research processor for the duration of the study
Exclusion Criteria	• Unrealistic expectations regarding potential benefits, risks and limitations of the investigational device as determined by the investigator • Unwillingness or physical / cognitive inability of subject to comply with all investigational requirements as determined by the investigator • < 50% words correct AzBio Sentence Test in quiet in either ear using the Naída CI M90 research processor
Primary Study/Efficacy Objective	The primary objective is to demonstrate that speech recognition in quiet on a Naída CI L90 processor is no worse than speech recognition in quiet on the currently approved Naída CI M90 processor for speech understanding in quiet.

Primary Study/Efficacy Endpoint	AzBio sentence scores in quiet at Baseline with AutoSense OS 5.0 and BSE features on a Naída CI L90 processor as compared to AzBio sentence scores in quiet at Baseline with a currently approved Naída CI M90 processor.
Secondary Study Objective	The secondary objectives are • To demonstrate non-inferiority of the Naída CI L90 processor, relative to the currently approved Naída CI M90 processor for speech understanding in noise. • To demonstrate improved localization ability of the Naída CI L90 processor with the Binaural Spatial Enhancement features "on" versus features "off".
Secondary Study/Efficacy Endpoint	The secondary endpoints are • AzBio sentence scores in noise at Baseline with AutoSense OS 5.0 and BSE features on a Naída CI L90 processor as compared to AzBio sentence scores in noise at Baseline with currently approved software on a Naída CI M90 processor. • Sound localization ability of the Naída CI L90 processor with the BSE features "on" versus features "off.
Safety Objective	The primary safety objective is to evaluate whether there are adverse events related to the use of the Naída CI L90 processor that impact device safety during chronic device use.
Safety Endpoints	Absence of unanticipated adverse device effects related to use of the Naída CI L90 processor.
Supporting Data	Analysis of customized sponsor developed subject self-assessment questionnaire after 14-21 days of chronic use with the Naída CI L90 processor in everyday listening situations.
Study Schedule & Duration	14-21 days.
Study Monitoring	Advanced Bionics, LLC 28515 Westinghouse Place Valencia, CA 91355 [redacted]

Statistical Analyses	Descriptive statistics will be provided, consisting of means, standard deviations, and number of observations for continuous variables (primary and secondary endpoints) and frequency and percentages for categorical variables (safety endpoint). Two-sided 95% confidence intervals will be provided for means and percentages, if applicable. The non-inferiority analysis of the primary efficacy endpoint (AzBio sentence scores in quiet) and secondary efficacy endpoint (AzBio Sentence scores in noise) will be based on a paired t-test at one-sided 0.025 significance level. Improvement (superiority) in localization scores in quiet with BSE Features [redacted] "on" as compared to BSE Features "off" using a Naida CI L90 processor will be assessed using a paired t-test at one-sided 0.025 significance

2.0 Glossary and Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
AutoSense OS	AutoSense OS is a digital signal processing platform that automatically coordinates the settings of device features of the Naída CI family processors, also referenced as AutoSense.
Binaural Spatial Enhancement (BSE)	BSE is a feature set that focuses on enhancing speech in noise clarity and localization. [redacted]
BTE	Behind-the-ear
CIP	Clinical Investigation Plan
CRF	Case Report Forms
Front End Processing features (FEPs)	Sound cleaning features applied prior to the electrical signal processing
HiResolution™ (HiRes) Bionic Ear cochlear implant system	An implantable medical device system designed to provide individuals who have severe-to-profound hearing loss with access to sound and improved recognition 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.
Hz	Hertz
[redacted]	[redacted]
Naída CI L90 (L90)	Investigational sound processor also abbreviated as “L90 processor”. [redacted]
Naída CI M90 (M90)	Currently approved sound processor used as comparator, also abbreviated as “M90 processor”. The M90 sound processor may also be referenced by its commercial name “Marvel”.

NoahLink Wireless	Wireless interface for cochlear implant sound processor fitting and programming
ListPlayer	The Listplayer platform is a proprietary, validated Advanced Bionics software used for speech recognition and localization testing
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SNHL	Sensorineural hearing loss
SNR	Signal-to-noise ratio
Sound Processor	The external part of a cochlear implant system that captures sound and converts it to digital information, also referred to as processor.
SPL	Sound Pressure Level
[redacted]	
RMSE	Root Mean Square Error
Target CI	The fitting software platform for the Naída CI M90 and the Naída CI L90 fitting and programming. [redacted] The version used to program the L90 processor will be investigational (Target CI v.1.6) while the commercially (Target CI v.1.5) available version will be used to program the M90.
UADE	Unanticipated Adverse Device Effect

3.0 Background and Purpose of the Investigation

Advanced Bionics (AB) is introducing the next generation processor, Naída CI L90. This sound processor leverages the benefits of previous AB technology combined with the Phonak [redacted] platform. This update will enable several new or updated features such as AutoSense OS 5.0, including features such as Speech Enhancer and SpeechSensor, for everyday listening experience. This change also includes Binaural Spatial Enhancement (BSE), a feature set focused on improved spatial situational awareness through proprietary technology that allows devices on the two ears to work together. [redacted] The L90 processor is compatible with AB's existing implants (Clarion CII and newer) and sound processing strategies. AB's fitting software, Target CI version 1.6, will be a compatible version of fitting software that will be used with the Naída CI L90 sound processors.

The overall goal of this clinical study is to demonstrate the safety and efficacy of Naída CI L90 sound processor in users of the HiResolution Bionic Ear System. Hearing outcomes are expected to be similar with the Naída CI L90 processor as compared to the Naída CI M90 processor. Therefore, the study described herein uses a non-inferiority design to demonstrate non-inferiority of the Naída CI L90 processor, relative to the currently approved Naída CI M90 for sentence understanding in quiet and in noise. Additionally, the BSE features on the Naída CI L90

device will be evaluated to demonstrate superior spatial situational awareness using a localization task when BSE features are enabled, versus disabled.

4.0 Identification and Description of the Investigational Device

- The HiResolution™ Bionic Ear cochlear implant system consists of Internal components consist of an implantable electronics package and electrode array
- Externally worn sound processor
- Custom fitting software used to program the external sound processor

This study will enroll subjects who are already implanted with a HiResolution Bionic Ear System (HiRes 90K, HiRes 90K Advantage, HiRes Ultra or HiRes Ultra 3D and CII with HiFocus electrode).

4.1 Investigational Programming Software/Listening Program(s) and Feature(s)

4.1.1 AutoSense OS 5.0

[redacted]

4.1.2 Binaural Spatial Enhancement (BSE)

Binaural Spatial Enhancement (BSE) is a feature set that focuses on enhancing speech in noise clarity and localization.[redacted]

[redacted]

Table 2: BSE Feature Descriptions

[redacted]

BSE features can be manual enabled or disabled as needed by the audiologist in a fitting session to accommodate listener preference.

4.1.3 Target CI v.1.6 Fitting Software

A research version (1.6) of the Target CI fitting software will be used for the programming of the L90 processor and to adjust the programming features prior to downloading to the processor. This software is functionally similar to the currently approved Target CI v.1.5 fitting software, providing utilities for changes in stimulation and fitting parameters. The new version of Target CI software will not modify the parameters and operational principles governing stimulation safety (e.g. charge-balanced stimulation, charge density limits, current density limits, etc.).

AutoSense OS presets within the Target CI fitting software are the starting point for the fitting of the program, as discussed above. In addition, the software allows the audiologist to modify the presets for specific scene types and to create manual programs for use without AutoSense OS.

4.2 Investigational Hardware

4.2.1 L90 Processor Package

[redacted]



5.0 Study Design and Justification

This study uses a prospective within-subjects repeated-measures design. A within-subject repeated-measures study design is appropriate as it accommodates the heterogeneity that characterizes hearing-impaired populations. Acute speech recognition testing in quiet will be used to evaluate AutoSense OS 5.0 and BSE features on L90 processors using Target CI (v.1.6) fitting software (investigational device) as compared to the approved AutoSense OS 3.0 on M90 processors using Target CI (v.1.5) fitting software (control device). Statistical analyses will be used to determine if sentence perception with the investigational device is no worse than with the control device, supporting the non-inferiority hypothesis.

Localization performance supported by BSE features will also be evaluated with two "Feature On" manual programs: Statistical analysis of the localization outcome measures (i.e. slope of linear regression fit and RMSE between response and target angles) will be conducted to determine if performance in the "Feature On" conditions is statistically different (i.e. improved) relative to the "Feature Off" condition.

Finally, a chronic exposure period of 14-21 Days with the Naída CI L90 processors will be used to evaluate the investigational device in the subjects' everyday hearing environment.

Adverse events (AEs) 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 and two weeks after the participant completes the study.

6.0 Objectives

The primary objective of the proposed clinical study is to demonstrate that speech recognition in quiet with AutoSense OS 5.0 and BSE features on a L90 processor is no worse than speech recognition in quiet with currently approved AutoSense OS 3.0 on a M90 processor. Secondary objectives include A) a demonstration that speech recognition in noise with AutoSense 5.0 and BSE features on a L90 processor is no worse than speech recognition in noise with currently approved AutoSense OS 3.0 on a M90 processor and B) that enabling BSE features on the L90 processor significantly improve spatial awareness, demonstrated by comparison of localization outcome measures (i.e. slope of linear regression fit and RMSE between response and target angles)with the BSE features “On” versus “Off”.

7.0 Study Protocol

7.1 Subject Population and Selection Criteria

Advanced Bionics expects to fit up to 18 adult HiResolution Bionic Ear system users with the investigational device in this clinical study at up to 3 participating sites in the United States. Each study center will enroll no more than 2/5 (40%) of the subject population for the study. An individual is considered to be enrolled as a study participant once the informed consent document has been signed and dated. It is anticipated that a larger number of subjects will be enrolled in the study as some may not meet the inclusion / exclusion criteria. Prior to recruitment, written approval of the investigational plan and informed consent form will be obtained from the FDA and associated participating study center Institutional Review Boards (IRB). Study participants are required to meet the study inclusion criteria as determined by the Principal Investigator.

7.2 Inclusion and Exclusion Criteria

7.2.1 General Inclusion Criteria

- Ability to provide Informed Consent
- 18 years of age or older
- Bilateral users of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D and CII with HiFocus electrode).
- Minimum of 6 months of CI experience for each ear
- At least moderate open-set speech recognition abilities with each implant side, as defined by achieving a unilateral score of ≥ 50% words correct in the AzBio in quiet test using the Naída CI M90 research processor, for each implant side.
- English language proficiency as determined by the investigator
- Willingness to use a behind-the-ear research processor for the duration of the study

7.2.2 Exclusion Criteria

- Unrealistic expectations regarding potential benefits, risks and limitations of the investigational device as determined by the investigator
- Unwillingness or physical / cognitive inability of subject to comply with all investigational requirements as determined by the investigator

- < 50% words correct AzBio Sentence Test in quiet in either ear using the Naída CI M90 research processor

7.3 Study Endpoints

The purpose of the proposed study is to evaluate efficacy objectives. Speech recognition and subjective outcome data will be collected during the study. The primary efficacy endpoints are the AzBio sentence scores in quiet at Baseline with AutoSense OS 5.0 and Binaural Spatial Enhancement (BSE) features on a Naída CI L90 processor as compared to AzBio sentence scores in quiet at Baseline with currently approved software on a Naída CI M90 processor.
Secondary endpoints include:

- AzBio sentence scores in noise at Baseline with AutoSense OS 5.0 and BSE features on a Naída CI L90 processor as compared to AzBio sentence scores in noise at Baseline with currently approved software on a Naída CI M90 processor.
- Sound localization ability of the Naída CI L90 processor with the BSE features “on” versus features “off.

7.4 Study Procedures

Advanced Bionics staff may be present during study procedures for the purpose of guiding investigators with regards to per protocol performance of these procedures. As this potentially involves contact with study subjects, Advanced Bionics staff will conduct these activities in a way that they do not bias data integrity. No study procedures will be performed by Advanced Bionics staff.

7.4.1 Speech Recognition Measures:

Speech recognition testing will be conducted in a single- or double-walled sound booth. The AzBio Sentence Test will be used to assess performance. The materials include both sentence tests and calibration signals to insure appropriate presentation levels of speech and background noise. Individual ear scores using AzBio Sentences in quiet will be used as the test metric to determine eligibility.

The AzBio Sentence Test (Spahr et al., 2012) is a validated test of open-set sentence recognition ability. The test will be administered in quiet at 60 dBA (target 0° azimuth). AzBio Sentence tests will be used to evaluate the L90 and M90 processors in quiet and in noise. The AzBio Sentence Testing in Quiet will be administered at 60 dBA at 0° azimuth. The AzBio Sentence Test in noise will be administered at 60 dBA + 5 dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth. The test is scored as total number of words correct which will be expressed for reporting as percentage correct. The sentence tokens include both male and female speakers.

7.4.2 Localization Testing

Localization testing is a specialized task not available in most clinics. There are minor differences in hardware configurations across centers, which are not easily modified. Thus, we provide minimum requirements for localization testing and centers may meet or exceed these

requirements. All configurations are compatible with calculating our described localization outcome measures (i.e. slope and RMSE). Test sites selected for this study will have access to a soundbooth or chamber capable of conducting localization testing. The test environment will utilize a minimum of 11 loudspeakers (sequentially numbered) spaced evenly over an angular range of at least 140 degrees, not to exceed 180 degrees. The center loudspeaker will be located at 0 degrees azimuth, relative to the seated subject, with a minimum of 1 meter from subject to loudspeaker. Custom software (i.e. Listplayer) will be used by all test sites for calibration, training, testing, and reporting. The test stimulus is a pink noise, lowpass filtered at 800 Hz, with a presentation level of 65 dBA with loudness roving (+/-3 dB) applied to each trial. Equal number of presentations from each loudspeaker will be delivered, with a minimum of 55 total number of presentations (number of presentations per loudspeaker x number of loudspeakers). The presentation order will be randomized and controlled by the software. After each presentation, the subject will identify the loudspeaker number believed to be the source of the signal. The tester will record the response in the software prior to delivery of the next signal. The software will capture presentation loudspeaker number and response for each trial. Results will be saved for each testing condition and slope and RMSE values of the BSE “On” and “Off” conditions will be calculated after testing has been completed.

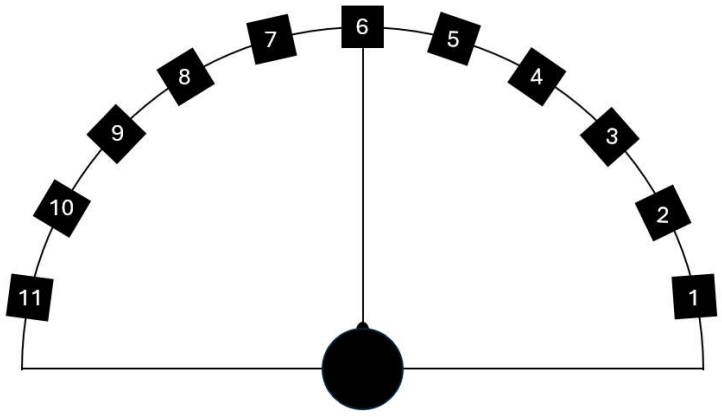


Figure 2. Example of Localization Loudspeaker Set-up: A minimum of 11 loudspeakers spaced evenly over an angular range of at least 140 degrees, not to exceed 180 degrees. The center loudspeaker will be located at 0 degrees azimuth, relative to the seated subject, with a minimum of 1 meter from subject to loudspeaker.

7.4.3 Questionnaires

Subjects will complete a customized sponsor developed self-assessment questionnaire about their listening experience with their current sound processor. This same questionnaire will be administered following a 14–21-day chronic evaluation period with the Naída L90 processors. This evaluation period is intended to determine if the devices are acceptable for use in everyday listening situations. As is common practice for clinical programming sessions, the audiologist may adjust program parameters based on listening preferences of each subject. At the conclusion of the chronic evaluation period, subjects will complete the questionnaire and return it, along with

investigational equipment, to the investigator. The results of the baseline and final questionnaire will be analyzed to assess any differences in acceptability.

Following completion of the trial, subjects will return to use of their commercially approved sound processor(s) utilized prior to the trial.

7.5 Study Visits and Visit Windows

Signed Informed Consent is to be obtained prior to the conduct of any study procedures. Baseline information consists of collection of participant demographics, hearing and pertinent medical history (e.g. etiology of hearing loss, date of birth, gender, duration of severe to profound hearing loss).

7.6 Study Inclusion Screening

Subjects will be evaluated prior to the start of the Baseline visit to determine at least moderate open-set speech recognition abilities with implant in each individual implanted ear, as defined by achieving a score of ≥ 50% words correct in the AzBio Sentence Test in quiet using a Naída CI M90 research processor.

7.6.1 Naída CI M90 Fitting

Subjects will be fitted with M90 research processors with T-mic using Target CI version 1.5. AutoSense OS 3.0 will be used with M and T levels, strategy, ClearVoice and SoftVoice settings set the same as the subject's own sound processor. IDR will be set to default. Slight adjustments may be made to M and T levels, as needed.

7.6.2 Study Inclusion Screening

The AzBio Sentence Testing in Quiet will be administered at 60 dBA at 0° azimuth using the AutoSense OS automatic program on the right and left M90 processors, individually. The non-test ear sound processor will be removed during testing.

7.7 Baseline Visit

If the subject meets all inclusion criteria, the following test measures will be administered at the Baseline Visit:

7.7.1 Baseline Self-Assessment Questionnaire

Subjects will complete a customized self-assessment questionnaire to determine subjectively reported experience in various listening scenarios.

7.7.2 Naída M90 Speech Recognition Testing

7.7.2.1 AzBio Sentence Testing with AutoSense OS 3.0 on the M90 processor in Quiet

The AzBio Sentence Test in quiet will be administered at 60 dBA at 0° azimuth using the AutoSense OS 3.0 automatic program on the M90 processors, bilaterally. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

7.7.2.2 AzBio Sentence Testing with AutoSense OS 3.0 on the M90 processor in Noise

The AzBio Sentence Test in noise will be administered at 60 dBA + 5 dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth using the AutoSense OS 3.0 automatic program on the M90 processors, bilaterally. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

7.7.3 Naída CI L90 Fitting

Subject will be fitted with L90 research processors with T-mic using Target CI version 1.6. M and T levels, strategy, ClearVoice and SoftVoice settings will be transferred from the M90 research processor fitting session. IDR will be set to default. AutoSense OS feature settings will be set at default and AGC setting and side beamformer will be set to [redacted]. Three additional manual programs will be added:

(1) **"Feature Off" program**: [redacted] set to "Off".

(2) **"Feature On"** [redacted] set to "Off".

(3) **"Feature On"** [redacted] set to [redacted]".

7.7.4 Naída CI L90 Speech Recognition Testing

7.7.4.1 AzBio Sentence Testing with AutoSense OS 5.0 on the L90 processor in Quiet

The AzBio Sentence Test in quiet will be administered at 60 dBA at 0° azimuth using the AutoSense OS 5.0 automatic program on the L90 processors, bilaterally. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

7.7.4.2 AzBio Sentence Testing with AutoSense OS 5.0 on the L90 processor in Noise

The AzBio Sentence Test in noise will be administered at 60 dBA with +5dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth using the AutoSense OS 5.0 automatic program on the L90 processors, bilaterally. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

7.7.5 Naída CI L90 Localization Testing

7.7.5.1 Localization Testing on the L90 processors "Feature Off" program in Quiet

A practice set will be conducted in this program, prior to the evaluation, allowing the subject to learn the localization task.

Localization in quiet testing in this program will be administered per the description in section 7.4.2.

7.7.5.2 Localization Testing on the L90 processors "Feature On" [redacted] program in Quiet

Localization in quiet testing in this program will be administered per the description in section 7.4.2.

7.7.5.3 Localization Testing on the L90 processors "Feature On' [redacted] program in Quiet

Localization in quiet testing in this program will be administered per the description in section

7.7.6 Adverse Event Assessment

An adverse event assessment will be completed by the investigator at the end of the baseline visit.

7.8 Chronic Evaluation Period

7.8.1 Chronic Period Instructions

Prior to starting the chronic evaluation period, the "Feature Off" and "Feature On" programs will be deleted from the L90 processors and subjects will be able to customize AutoSense OS and program settings based on their preference. BSE features will be enabled in the AutoSense OS program for chronic use. Slight adjustments may be made to the programming, as needed. The subject will wear the Naída CI L90 research devices for 14-21 days during their everyday activities.

Once the subject has returned the processors to the study site, the Investigator will connect the processors to the Target CI fitting software and create a session to document the chronic use period.

7.8.2 Follow-Up Self-Assessment Questionnaire

Subjects will complete a customized self-assessment questionnaire on paper or through the EDC system, 14 to 21 days after the baseline visit. If completed on paper, the questionnaire will be returned with the investigational devices.

7.8.3 Adverse Event Assessment:

An adverse event assessment is completed by the investigator at the end of the chronic period.

7.8.4 Device Return

Subjects will be provided a FEDEX envelope and airbill at the baseline visit and will return the investigational L90 processors after 14 to 21 days of chronic use.

Table 3: Summary of Visit Activities

Procedure		Baseline Visit	Chronic Period
Informed Consent		X	
Demographics & Audiological History		X	
AutoSense on the M90 Processor (tested unilaterally)	AzBio in Quiet	X	
Confirmation of Eligibility		X	
Custom Non-standardized Self-Assessment Questionnaire		X	X
Tests conducted bilaterally			
AutoSense on the M90 Processor	AzBio in Quiet	X	
	AzBio in Noise	X	
AutoSense on the L90 Processor	AzBio in Quiet	X	
	AzBio in Noise	X	
Calm situation “Feature Off” program on the L90 Processor	Localization Evaluation	X	
Calm situation “Feature On” program [redacted] on the L90 Processor	Localization Evaluation	X	
Calm situation “Feature On” program on [redacted] the L90 Processor	Localization Evaluation	X	
Adverse Event Assessment		X	X
Device Accountability		X	X

7.9 Withdrawal of Subjects

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 have the right to discontinue study participants. Participants can be discontinued for the following reasons:

- Voluntary withdrawal of consent made by the participant
- A safety concern identified by the Principal Investigator, the Sponsor, or any third party
- Inability of the subject to perform the tasks necessary to provide usable data for the study
- Failure to respond after three documented attempts to contact the subject (lost to follow-up). Potential reasons will be documented.

Once a subject is withdrawn or discontinued, they will be required to return the Naída CI L90 sound processor utilized for the study. Subjects who withdraw or who are discontinued from the study will be reported accordingly to the Institutional Review Board. If a subject was discontinued because of a device-related adverse event or serious adverse event (SAE), the subject must be followed until the adverse event is resolved, the point at which the subject withdraws consent, 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 Capture system the disposition of each enrolled subject (e.g., completed study, withdrew, discontinued, lost to follow-up). Additional subjects may be enrolled if the minimum sample size cannot be reached due to withdrawn, discontinued or lost to follow-up subjects.

8.0 Statistics

8.1 General Considerations

A detailed Statistical Analysis Plan (SAP) will be developed and approved prior to analysis of the data. The following provides a summary overview of analyses to be performed. Statistical deviations from the study protocol and/or from the final SAP will be described in the clinical investigation report.

The sample size of 18 subjects will include subjects that meet inclusion/exclusion criteria. The sample size includes an allowance for dropouts/unevaluable subjects.

The following data will be collected and evaluated as part of this study:

- Acute speech recognition testing in quiet (primary efficacy endpoint) will be used to evaluate AutoSense OS 5.0 and BSE features on L90 processors using Target CI (v.1.6) fitting software (investigational device) as compared to the approved AutoSense OS 3.0 on M90 processors using Target CI (v.1.5) fitting software (control device).
- Speech recognition testing in noise (secondary efficacy endpoint) will be evaluated with the L90 processors as compared to the M90 processors.
- Localization performance in quiet (secondary efficacy endpoint) supported by BSE features will also be evaluated with two “Feature On” manual programs: 1) SyncAGC enabled, 2) SyncAGC + IABF enabled compared to a “Feature Off” program, with BSE features disabled using a Naída L90 processor.
- Customized sponsor developed self-assessment questionnaire (supporting data) after 14-21 days of chronic use with the Naída CI L90 processors in everyday listening situations.
- Adverse events, including unanticipated adverse device effects (safety endpoint), related to use of the Naída CI L90 processor.

Descriptive statistics will be provided, consisting of, means, standard deviations, and number of observations for continuous variables (primary and secondary endpoints and frequency and percentages for categorical variables (safety endpoint). Two-sided 95% confidence intervals will be provided for means and percentages, if applicable.

Potential for bias during this clinical investigation has been minimized by expected conduct under the terms of an approved clinical investigation plan, use of specific inclusion and exclusion criteria, careful definitions for clinical investigation procedures and outcomes and prospectively defined methods of data analysis.

No interim analysis is planned for this study.

8.1.1 Data Analyses

8.1.1.1 Efficacy Endpoints

The primary efficacy endpoint is AzBio sentence scores in quiet at Baseline with AutoSense on a Naída CI L90 processor (Investigational) as compared to AzBio sentence scores in quiet at Baseline with a currently approved Naída CI M90 processor (Control). The primary objective is to demonstrate that speech recognition in quiet on a Naída CI L90 processor is no worse (non-inferior) than speech recognition in quiet on the currently approved Naída CI M90 processor for speech understanding in quiet. The non-inferiority analysis will be based on a paired t-test looking at the differences in scores calculated using the Investigational scores minus the Control scores at the baseline visit. A one-sided hypothesis test will be used at a significance level (alpha [a]) = 0.025 The following are the null (H_0) and alternative (H_1) statistical hypotheses:

$$H_0: \mu_\Delta \leq -0.10 \text{ versus } H_1: \mu_\Delta > -0.10$$

where μ_Δ is the mean of the paired difference ((AutoSense OS 5.0 on L90 [Investigational] – AutoSense OS 3.0 on M90 [Control]) in scores on the AzBio sentence test in quiet at Baseline. A non-inferiority bound of 0.10 (10%) was selected for the AzBio test based on procedures used in previous studies [redacted]. Statistically significant test results that reject the null hypotheses, indicating that the means of the paired differences is greater than -0.1 (-10%) for AzBio in quiet mode, will support that the Investigational device is non-inferior to the Control device.

The first secondary efficacy endpoint is AzBio Sentence scores in noise at Baseline with AutoSense OS 5.0 and BSE features on a Naida CI L90 processor (Investigational) as compared to AzBio sentence scores in noise at Baseline with a currently approved Naida CI M90 processor (Control). The secondary study objective is to demonstrate non-inferiority of the Naída CI L90 processor, relative to the currently approved Naída CI M90 processor for speech understanding in noise. The non-inferiority analysis will be based on a paired t-test and hypotheses similar to the primary efficacy endpoint (i.e., -0.10 (-10%) non-inferiority margin; one-sided significance level = 0.025).

The primary and first secondary efficacy endpoints will first be assessed for non-inferiority. If non-inferiority is met for both endpoints, then they will be assessed for superiority in a hierarchical manner. This hierarchical approach to hypothesis testing will control the study's overall Type I error rate (see Section 8.1.1.2 for more details).

The 2nd secondary efficacy endpoint is localization scores in quiet with BSE Features [redacted] "on" as compared to BSE Features "off" using a Naida CI L90 processor. Statistical analysis of the localization outcome measures (i.e. slope of linear regression fit and RMSE

between response and target angles) will be conducted to determine if performance in the "Feature On" condition is statistically different (i.e., improved; superior) relative to the "Feature Off" condition. The superiority analysis will be based on a paired t-test looking at the differences in slopes (and RMSEs) between BSE "Features On" minus "Features Off". A one-sided hypothesis test will be used at a significance level (alpha [a]) = 0.025. The following are the null (H_0) and alternative (H_1) statistical hypotheses with respect to slope and RMSE, respectively:

$$\text{Slope: } H_0: \mu_\Delta \leq 0 \text{ versus } H_1: \mu_\Delta > 0$$
$$\text{RMSE: } H_0: \mu_\Delta \geq 0 \text{ versus } H_1: \mu_\Delta < 0$$

where μ_Δ is the mean of the paired difference (Features On – Features Off) in slopes (or RMSEs) of the localization responses in quiet at Baseline using a Naida CI L90 processor. Statistical testing with respect to slope and RMSE will be performed independently (separately). Statistically significant test results that reject the null hypothesis for slope, indicating that the mean of the paired differences with respect to slope is greater than 0, will support that BSE Features "on" condition is superior (improved) relative to the Features "off" condition with respect slope. Statistically significant test results that reject the null hypothesis for RMSE, indicating that the mean of the paired differences with respect to RMSE is less than 0, will support that BSE Features "on" condition is superior (improved) relative to the Features "off" condition with respect RMSE.

Subgroup and Covariate/Confounding Analyses

Additional analyses will be conducted to assess any differences based on age of onset (as categorical variable) or duration of sensorineural hearing loss (SNHL) (as categorical variable). An analysis of variance (ANOVA) will be used to model the paired differences (Investigational – Control) of AzBio sentences in quiet with age of onset and duration of SNHL as independent variables. The analysis will be repeated for AzBio sentences scores in noise and localization scores in quiet (i.e., features On – Features Off). The results will also be presented by age of onset and duration of SNHL.

Assessment of Homogeneity (Poolability)

The study plans to enroll subjects from up to 3 participating sites in the United States. Each study center will enroll no more than 2/5 (40%) of the subject population for the study. Analyses will be conducted to assess any differences across investigational sites (i.e., study centers). An analysis of variance (ANOVA) will be used to model the paired differences (Investigational – Control) of AzBio sentence scores in quiet with study center as independent variable. The analysis will be repeated for AzBio sentence scores in noise and localization scores in quiet (i.e., Features On – Features Off). Lack of homogeneity will be declared if the p-value for the study center variable in the ANOVA model exceeds 0.10. If the effectiveness response is not homogenous across sites, the appropriate regression analysis will be done to determine if the lack of homogeneity is due to the study center or due to a possible imbalance in baseline characteristics of the subjects across study centers. If the study center effect is no longer significant at P<0.10

after adding the potentially unbalanced baseline covariates, then study center will not be considered a source of lack of homogeneity.

The efficacy results will also be presented by study center.

Handling of Missing Data

Since the primary and secondary efficacy endpoints are assessed at a single [i.e., the first (baseline)] visit, it is anticipated that there will be no (or very minimal) missing data and therefore efficacy analyses will be based on available data (i.e., missing data will not be imputed). If there is missing efficacy data, then a sensitivity analysis will be performed based on multiple imputation. Details regarding this sensitivity analysis will be provided in the detailed SAP.

The study includes a chronic evaluation period 14 to 21 days after the baseline visit with a subjective questionnaire. Therefore, a small possibility exists that some study participants will not complete the entire test protocol. Every attempt will be made to contact subjects who are non-compliant or lost to follow-up, and such attempts will be documented in the subject's study record. All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection. Given the study design, no safety and supportive data will be imputed.

8.1.1.2 Type 1 Error Control

The study will have one primary and two secondary efficacy endpoints. The study's overall Type 1 error (alpha) will be maintained at one-sided 0.025 level using a hierarchical test approach. Specifically, hypothesis testing will be performed at the one-sided 0.025 significance level in the following pre-specified order:

1. Non-inferiority on primary efficacy endpoint (i.e., AzBio sentence scores in quiet at Baseline with AutoSense on a Naída CI L90 processor as compared to AzBio sentence scores in quiet at Baseline with a currently approved Naída CI M90 processor)
2. Non-inferiority on 1st secondary efficacy endpoint (i.e., AzBio Sentence scores in noise at Baseline with AutoSense on a Naida CI L90 processor as compared to AzBio sentence scores in noise at Baseline with a currently approved Naida CI M90 processor)
3. Superiority on 2nd secondary efficacy endpoint (i.e., Localization scores in quiet with BSE Features [redacted] "on" as compared to BSE Features "off" using a Naida CI L90 processor) with respect to slope of linear regression.
4. Superiority on 2nd secondary efficacy endpoint (i.e., Localization scores in quiet with BSE Features [redacted] "on" as compared to BSE Features "off" using a Naida CI L90 processor) with respect to RMSE of linear regression.
5. Superiority on primary efficacy endpoint
6. Superiority on 1st secondary efficacy endpoint

Specific claims will be made based on the above (in order) testing of primary and secondary efficacy endpoints; however, once (if) statistical significance is not met for a hypothesis test/endpoint, then formal statistical testing for any subsequent hypothesis/endpoint will not be performed for labeling claims purposes.

8.1.1.3 Analyses of Individual Results

A critical difference score will be used to determine whether individual subjects demonstrate a significant decrease in performance between the Investigational (AutoSense on a Naída CI L90 processor) and Control (Naída CI M90 processor) conditions. Specifically, the criterion value for the critical difference score will be based upon the test-retest variance on the AzBio test. Gifford (2008) provided a set of data on 35 listeners for the AzBio sentences, wherein two lists of sentences were presented one after the other to cochlear implant recipients. Based on those data, the expected variability between lists has a standard deviation σ of 3.8%. The critical difference score can be computed based on the assumption that (1) the difference scores have a normal distribution, and (2) the difference scores are deemed significant if, under the null hypothesis, the probability of the difference score exceeding the critical score is 1%. Under these assumptions, the critical improvement (or decrement) score CS is equal to:

$$CS = \sigma * b$$

In the above equation, b = 2.33, the percentile of the normal curve corresponding to the desired values of $\alpha = 0.01$, one-tailed test. Using Gifford's σ value, the critical difference score for AzBio sentences is 8.9%.

The number and percentage of subjects exceeding, within, and below the critical difference (Investigational - Control) score will be tabulated. Further the difference between the two conditions will be evaluated and classified as better for the Experimental condition, the same for both conditions, or better for the Control condition. A two-sided exact binomial test will be used to evaluate the null hypothesis that the distribution of subjects showing a performance difference (Investigational is better or Control is better) is distributed equally. This analysis will provide an additional indication of the efficacy of AutoSense on a Naída CI L90 processor relative to Naída CI M90 processor based upon individual data.

8.1.1.4 Safety Endpoint

The primary safety objective is to evaluate whether there are adverse events related to use of the Naída CI L90 processor that impact device safety during chronic device use. The incidence, nature and severity of adverse events related to use of the Naída CI L90 during chronic device use will be summarized using descriptive statistics (frequency and percentages). The study's safety endpoint is absence of unanticipated adverse device effects (UADEs) related to use of the Naída CI L90 processor. The safety endpoint will be summarized by providing the total number of UADEs and the number and percentage of subjects free of UADEs related to use of the Naída CI L90 processor.

8.1.1.5 Supporting Data

Data from the customized subject self-assessment questionnaire after 14-21 days of chronic use with the Naída CI L90 processor in everyday listening situations will be analyzed descriptively using frequency and percentages for categorical variables.

8.2 Sample Size Justification

A total sample size of 18 subjects is planned for this study based upon efficacy and safety considerations. Previous specific data were used to estimate the standard deviations (SD) for the paired L90-M90 differences. The primary efficacy objective is to demonstrate non-inferiority of AutoSense 5.0 on the L90 processor compared to AutoSense 3.0 on the M90 processor for the AzBio sentence test in quiet mode based on a paired t-test. The primary efficacy analyses will test the null hypothesis (H_0) that the mean of the paired differences (μ_Δ) in AzBio sentence scores in quiet mode (AutoSense 5.0 on L90 – AutoSense 3.0 on M90) are less than or equal to -10 percentage points, and alternative hypothesis (H_1) that m_D in AzBio sentence scores in quiet mode are greater than -10 percentage points. The statistical null (H_0) and alternative (H_1) hypotheses in mathematical notation are the following:

$$H_0: \mu_\Delta \leq -10\% \quad \text{versus} \quad H_1: \mu_\Delta > -10\%$$

Rejecting the null hypothesis at the one-sided 0.025 significance level will demonstrate that there is sufficient statistical evidence to conclude that mean difference, μ_Δ, is greater than -10 percentage points and will be considered to have shown that L90 is non-inferior to M90 with respect to AzBio sentence test in quiet mode.

The non-inferiority analysis of the 1st secondary efficacy endpoint (AzBio sentence scores in noise) will be based on a paired t-test and hypotheses similar to the primary efficacy endpoint (i.e., -0.10 (-10%) non-inferiority margin; one-sided significance level = 0.025). The superiority analysis of the 2nd secondary efficacy endpoint [localization responses (i.e., slope and RMSE of linear regression)] will be based on a paired t-test looking at the differences in slopes (and RMSE) between BSE “Features On” minus “Features Off”. A one-sided hypothesis test will be used at a one-sided significance level (alpha [a]) = 0.025.

Previous data supported 6.24% SD for the primary efficacy endpoint [AzBio sentence scores in quiet] (labelled 1 below) of the paired differences, 6.61% SD for the first secondary efficacy endpoint [AzBio sentence scores in noise] (labelled 2 below) of the paired differences, and 0.17 SD for the second secondary efficacy endpoint [localization responses (i.e. slope of linear regression)] (labelled 3 below) of the paired differences . As shown in Table 4 below, based on a sample size of 15 subjects (i.e., 15 pairs) there is >90% power to demonstrate non-inferiority (N-I) at one-sided 0.025 significance level for the primary efficacy endpoint and first secondary efficacy endpoint assuming the true mean paired difference for both endpoints is 0%. Based on a sample size of 15 subjects, there is >80% power to demonstrate superiority at one-sided 0.025 significance level for the primary efficacy endpoint and first secondary efficacy endpoint assuming the true mean paired difference is 6.24% and 6.61%, respectively (based on previous data). Based on a sample size of 15 subjects, there is >90% power to demonstrate superiority at one-sided 0.025 significance level for the second secondary efficacy endpoint assuming true mean of paired differences in slope is 0.4 (based on previous data).

A total of 18 subjects will be enrolled in order to accommodate up to three unevaluable subjects.

Table 4: Paired t-tests to reject the null hypotheses for non-inferiority (N-I) and superiority

	Reach N-I			Reach Superiority		
	1 AzBio sentence scores in quiet	**2 AzBio Sentence scores in noise**	**3 localization responses (i.e. slope of linear regression)**	**1 AzBio sentence scores in quiet**	**2 AzBio Sentence scores in noise**	**3 localization responses (i.e. slope of linear regression)**
One-sided significance level, α	0.025	0.025	NA	0.025	0.025	0.025
Null hypothesis mean difference, μ_0	-10%	-10%	NA	0%	0%	0
Alternative mean difference, μ_A	0%	0%	NA	5.02%	5.32%	0.4
Paired SD, σ	6.24%	6.61%	NA	6.24%	6.61%	0.17
Effect size, $\delta = \lvert\mu_A - \mu_0\rvert / \sigma$	1.6	1.5	NA	0.80	0.80	2.4
Power (%)	>99.9	>99.9	NA	82.5	82.6	>99.9
N pairs	15	15	NA	15	15	15

Above calculations are based on PASS (v15.0.13) software.

A sample size of 15 evaluable subjects can provide sufficient data for determining the safety of the investigational device. If no UADEs are observed in 15 subjects (observed event rate -+0%), then 18.1% is the upper bound for a one-sided 95% Exact (Clopper-Pearson) confidence interval on this event rate. Therefore, with an observed event rate of 0% based on a sample size of 15, we would be 95% confident that the true event rate for the population of interest is less than 18.1%.

8.3 Analysis Populations

- **Full Analysis Set (FAS)** includes all subjects meeting eligibility criteria with evaluable baseline data. The FAS will be the primary analysis population for the efficacy analyses.
- **Per-protocol (PP)** population includes all FAS subjects with no major protocol deviations. The PP population will be a secondary analysis population for the efficacy analyses.
- **Safety population** includes all subjects meeting eligibility criteria fitted with the investigational device (Naída CI L90 Processor). The Safety population will be the primary analysis population for the safety and supporting data analyses.

Table 5: Major Protocol Deviations

	Baseline speech recognition scores that do not meet inclusion criteria of at least moderate open-set speech recognition abilities with implant in each individual implanted ear, as defined by achieving a score of ≥ 50% words correct in the AzBio Sentence Test in quiet using a Naída CI M90 research processor
Protocol deviations affecting data integrity of the primary endpoint	Speech recognition testing performed without removing sound processor from the non-test ear during unilateral AzBio in quiet test.
	Speech recognition testing performed without prior calibration of sound field levels to 74dB SPL.
	Speech recognition testing not performed at 0° azimuth.
	Speech recognition testing not performed with speech signals presented at 60 dBA.
	Speech recognition testing not performed in a minimum, a single-walled sound booth.
	Speech recognition testing not performed using two lists of AzBio sentences.
Protocol deviations affecting subject safety	Protocol deviations that result in a serious adverse event

8.4 Adverse Events and Device Deficiencies

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

All device-related and non-device-related adverse events (AEs) will be tracked and reported accordingly throughout the study as defined above in the investigational plan and in accordance with requirements of an IDE investigation. The AEs will be recorded and tracked between completion of the informed consent form (signed and dated) and two weeks after the participant's last study visit. The number and percent of all subjects experiencing adverse events

will be summarized by type, status and frequency of event. Adverse Events will be recorded and will include but are not limited to the following information [refer to Appendix B for Case Report Forms (CRFs)]:

Table 6: Adverse Event Definitions and Classifications

Term	Definitions
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. This includes the comparator if it is a medical device.
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. This definition includes events related to the investigational medical device or the comparator. This definition includes events related to the procedures involved. For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.
Anticipated Serious Adverse Device Effect (ASADE)	Any serious adverse effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Device Deficiency (DD)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: a) death b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function including chronic diseases, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function, c) foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment.

	Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
Serious health threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

8.4.1 Adverse Event Reporting

All adverse events and adverse device effects, serious and non-serious, will be recorded on the Adverse Event Report Case Report Form [CRF] (see Appendix B for all CRFs). Information to be recorded on the CRF should include, but is not limited to:

- Date of onset of the adverse event
- Description of the event, duration and severity
- Seriousness
- Relatedness
- Treatment/Intervention – course of action taken
- Outcome/Status (Resolved, Improved, Stable, Worse, Unchanged). In case of an SAE, the subject must be followed until the serious adverse device effect is resolved or no reasonable improvement is expected.

Investigators should immediately report any SAEs, SADEs and UADEs to Advanced Bionics at ClinicalResearch@AdvancedBionics.com. Evaluation of any SAE, SADE, or UADE will be conducted promptly. 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 reporting 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.

8.4.2 Anticipated Adverse Events

The risks associated with the investigational products include but are not limited to:

[redacted]



A complete listing of the risks can be found in Appendix A; all risks listed are considered anticipated Adverse Events. Risks are minimized by device safety testing but cannot be completely eliminated. At any time, subjects may discontinue use of the study sound processor, and return to using their own sound processor and baseline program. If subjects stop using the study sound processor during the study, they will be withdrawn from the study.

In all case, the event(s) will be recorded and the incidence of such events reported as part of the results analysis.

8.4.3 Device Deficiencies

Events that involve a device issue or observation need to be reported as Device Observations and Deficiencies (DODs) via the Electronic Data Capture system. Adverse event reporting takes precedent over DOD reporting. Therefore, it is not necessary to report an event as a DOD if it has already been reported as an AE because it led to a medical occurrence for the subject.

9.0 Informed Consent Process

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 and assistance in adapting the template to conform to local requirements (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 informed consent form to each subject.

Study subjects will receive a small payment at each visit for their time and effort and will be reimbursed for travel related cost.

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 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 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.

9.1 Health Insurance Portability and Accountability

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

10.0 Benefits and Risks

10.1 Benefits

Bilateral recipients of the HiResolution Bionic Ear System will realize significant benefit from an improved ability to locate sounds in space. Utilizing a proprietary ear-to-ear link, the Naída CI L90 sound processor BSE features enhance cues required to locate and track the location of sounds quickly, confidently, and accurately. The existing AutoSense OS in the processor allows listeners to seamlessly transition from one listening environment to another. With AutoSense OS combined with BSE, listeners are expected to maintain the level of speech understanding provided by our current device with improved sound source localization.

10.2 Risk related to Approved Products

The HiResolution Bionic Ear System is approved under P960058. Commercially approved Naída CI M batteries, battery chargers, T-mics [redacted] will be used in conjunction with both the Naída CI M90 and the CI L90. The risks associated with use of the approved products are contained in those products' instructions for use.

10.3 Risk related to Investigational Hardware

Risks associated with the investigational Naída CI L90 sound processor are covered in the Investigational Hardware Risk Analysis Report [redacted] The risk analysis contains the

determination that the benefit provided by this use-case outweighs any residual risk. The full report is available request upon request.

10.4 Risk related to Investigational Software

Risks associated with the investigational software and cybersecurity (including the sound processor firmware) are covered in the Risk Analysis Report for investigational software [redacted]. The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk. The full report is available upon request .

10.5 Risks related to Cybersecurity

Risks associated with cybersecurity of investigational products are covered in the Risk Analysis Report for investigational software [redacted]. The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk. The full report is available upon request.

11.0 Suspension or Premature Termination

11.1 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. If the study is prematurely terminated or suspended, the Principal Investigator will promptly inform study participants, provide the reason(s) for the termination or suspension and changes to the study visit schedule, as applicable. Any subjects that have not completed the study at the time of termination will be required to return the study sound processor and will resume using their personal sound processor.

No special follow-up procedures are required following the end or termination of the study as subject will be returning the study Naída CI L90 sound processor and returning to using their personal sound processor. The same applies to subjects who withdraw consent or are lost to follow-up. Should the study be temporarily halted, subjects will be asked to return the study Naída CI L90 sound processor until a determination is made whether the study will continue.

11.2 Criteria for Suspending or Terminating a Study Center

After the study begins, Advanced Bionics reserves the right to suspend enrollment of subjects at a study center or terminate a study center's participation in the study 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. Any subjects enrolled at this center that have not completed the study at the time of termination will be required to return the study sound processor and will resume using their personal sound processor.

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.

12.0 Monitoring, Device Accountability and Data Management

12.1 Monitoring Procedures

Independent monitoring of the study for clinical protocol compliance will be conducted periodically to oversee compliance with the regulatory and clinical aspects of the study. The Clinical Monitor will maintain current knowledge of the study through observation, review of study records and source documentation, and discussion of the study with the investigators and delegated study personnel. The study site will assist the monitor by providing access to all relevant study materials.

Site Initiation Training will be performed before a site enrolls subjects into the study. Periodic monitoring will be performed on-site as well as remotely throughout the study and a Close-Out Visit will be performed after all subjects at a site have completed the study. Details of clinical site monitoring are documented in a Clinical Monitoring Plan (CMP). The CMP describes in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.

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

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

Name/Title	Telephone	Email Address
[redacted]		

Address:

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

12.2 Device Accountability

Participants will be fitted with AutoSense on the investigational L90 processor package at their respective hearing care/implant centers. The investigational devices will be shipped with the following label: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use." The serial numbers for the investigational devices will be logged at the study site for each study participant. The statement "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use" will be placed onto the loaner laptop with the investigational Target CI software.

The Clinical Monitor or designee will conduct device accountability for the study, in accordance with the study-specific monitoring plan, to ensure that the Investigator maintains records for the following:

- Date of receipt,
- Identification of each investigational device (batch number/serial number or unique code),
- Expiry date, if applicable,
- Date or dates of use,
- Subject identification. e. g. study ID,
- Date on which the investigational device was returned/explanted from subject, if applicable, and
- Date on which unused, expired or malfunctioning investigational devices were returned to Advanced Bionics, if applicable

12.3 Data Management Procedures / Case Report Forms

Advanced Bionics will provide study centers with access to a study specific Electronic Data Capture (EDC) system meeting 21 CFR part 11 requirements. Details of the data management procedures are documented in the study specific Data Management Plan.

Data must be submitted according to protocol requirements for all enrolled subjects as soon as possible after the visit. Electronic Case Report Forms (eCRFs) provided for this study will be used to submit data (Appendix B). Each subject will be assigned a unique identifier at the time of the first visit, which will be used on all eCRFs.

The EDC database will be locked prior to analysis of the data and data will be retained indefinitely. Study Investigators will be provided with an electronic copy of the EDC database containing only the data from their subjects.

13.0 Statements of Compliance

13.1 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 as well as ISO 14155.

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 Agreement 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.

13.2 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 and any additional requirements imposed by the IRB.

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

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

13.3 Documents and Records

13.3.1 Pre-Study Documentation Requirements

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

- A copy of the Investigator Agreement, signed and dated by the Principal Investigator
- A signed and dated copy of the Clinical Trial Agreement
- Financial Disclosure for the Principal Investigator and Sub-Investigator(s), if applicable
- A copy of the 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)

13.4 Study Documentation

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 follow-up letters, 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.

13.5 Record Retention

All study records (e.g., protocol, IRB correspondence and approvals, eCRFs, patient records, consent forms, reports) must be maintained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonization (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. After this time records may be transferred to Advanced Bionics for indefinite storage.

If an Investigator opts to discontinue participation in the study, all records will be transferred to a mutually agreed designee (i.e., another Investigator). This transfer is subject to Advanced Bionics' approval and will be documented in writing with copies sent to Advanced Bionics. If an Investigator leaves the site at which the study was conducted, Advanced Bionics shall be contacted regarding the disposition of documents.

13.6 Inspection of Records

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

13.7 Study Funding

The study is funded by Advanced Bionics; financial agreements with the participating centers are addressed in a separate agreement.

14.0 Amendments and Deviations

14.1 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.

14.2 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.

14.3 Protocol Deviations

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

15.0 Publication Policy

This clinical study will be registered with clinicaltrials.gov and results will be made publicly available.

Advanced Bionics intends to publish the results of the clinical investigation in a peer reviewed journal. Authorship for the publication of the multi-center data will be jointly decided between Advanced Bionics and the Investigators. Further details of the publication policy will be governed by the Clinical Trial Agreement between Advanced Bionics and the participating institutions.

16.0 Bibliography

Gifford RG, Shallop JK, Peterson MA. (2008) Speech recognition materials and ceiling effects: Considerations for cochlear implant programs. Audiol Neurotol 13:263-271.

Spahr T, Dorman MF. (2004) Performance of subjects fit with the Advanced Bionics CII and Nucleus 3G cochlear implant devices. Arch Otolaryngol Head Neck Surg 130:624-628.

17.0 Study Sites, Investigators and External Organizations

17.1 Study Sites and Investigators under consideration

Up to 3 centers will be selected from the following:

Name of Center	Name of PI	Name and Address of IRB & Chairperson
[redacted]		

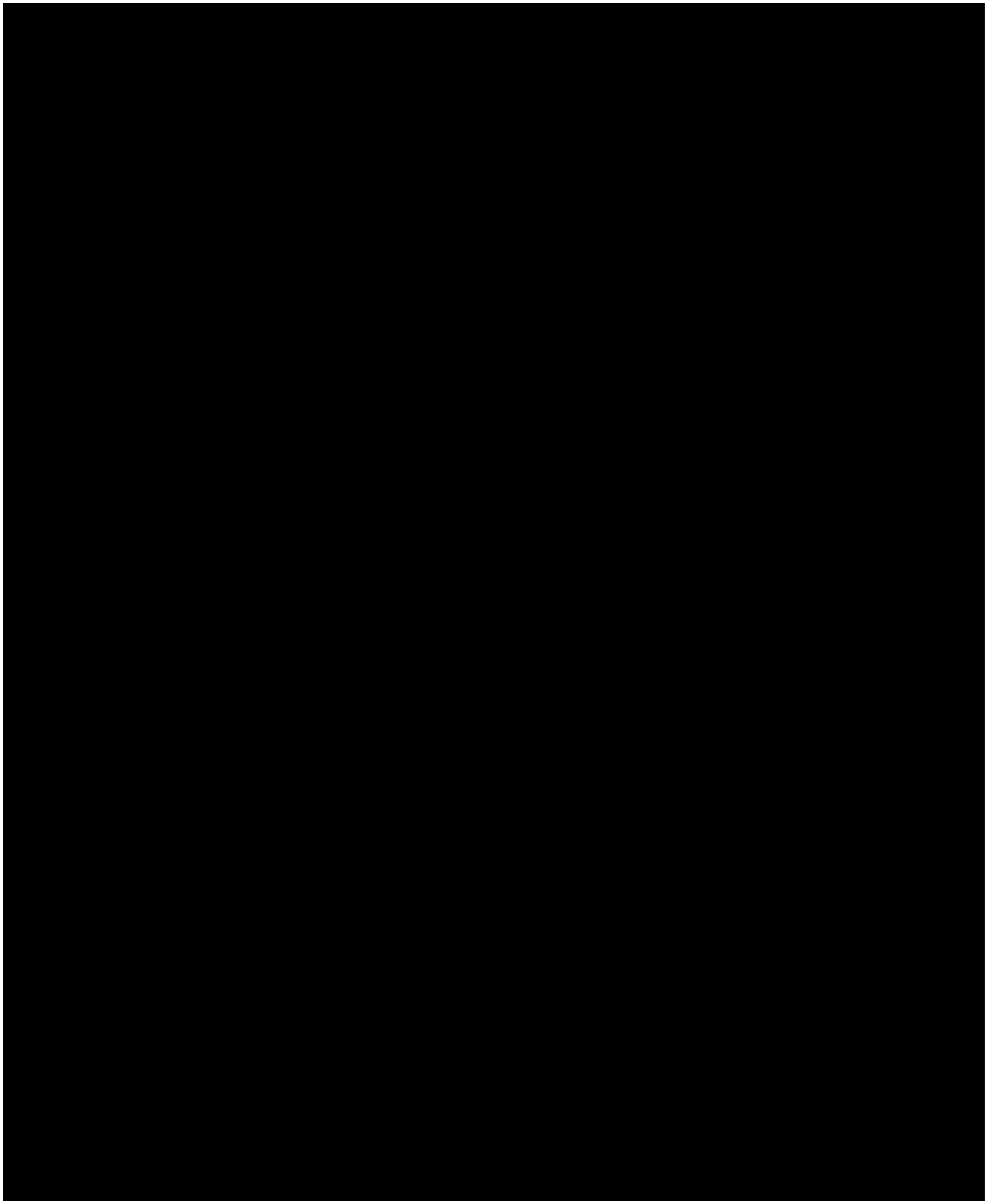
17.2 External Organizations

Organization	Role
Avania Clinical	Biostatistics

18.0 Revision History

Revision	Summary of Change	Date
1.0	Original Version	18 Sept 2024
1.1	Corrected minor clerical items, Updated company personnel names and contact info, Revised the ICF (Appendix B) to add cybersecurity risks and implement WCG IRB required standard ICF format, Removed RARs as an appendix in this document.	31 Oct 2024

19.0 CIP Sponsor Signature Page



20.0 CIP Investigator Signature Page

I, the undersigned, have read and understand the protocol specified above and agree on its content. I agree to perform and conduct the study as described in the protocol and in accordance with the relevant parts of ICH Guidelines for GCP, ISO 14155, the Declaration of Helsinki, the Declaration of Helsinki, and the pertinent individual country laws/regulations applicable in USA. In addition, I assume responsibility for protocol compliance for persons to whom I delegate study related tasks.

Name of the Principal Investigator, position, study center location: _____

Date: _____ **Signature:** _____