# Evaluation of AutoSense OS on a Naída CI M90 Sound Processor Programmed with Target CI Fitting Software in Adult Users of the HiResolution Bionic Ear System

INVESTIGATIONAL PLAN CR1218
PIVOTAL IDE

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Advanced Bionics, LLC
28515 Westinghouse Place
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## Investigator's Signature Page

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|---|---|
| Study Center: | |

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 the ICH Guidelines for GCP, ISO 14155, the Declaration of Helsinki, and the pertinent individual country laws/regulations.

Principal Investigator Name:

Principal Investigator Signature: _____

Signature Date: _____

## TABLE OF CONTENTS

## 1.0 Protocol Synopsis

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| *Study Title* | Evaluation of AutoSense OS on a Naída CI M90 Sound Processor Programmed with Target CI Fitting Software in Adult Users of the HiResolution™ Bionic Ear System |
| *Sponsor* | Advanced Bionics, LLC |
| *Investigational Device* | AutoSense Operating System on an investigational Naída CI M90 Processor programmed using investigational Target CI software |
| *Study Design* | Prospective within-subjects repeated-measures study |
| *Study Population* | 24 adult users implanted with a HiResolution Bionic Ear System (HiRes 90K™, HiRes 90K ™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D)<br>Subjects will be enrolled in 2 cohorts (12 per cohort):<br>- Aidable residual hearing (ARH, 12 subjects)<br>- Electric only (EO, 12 subjects) |
| *Inclusion Criteria All Cohorts* | • Ability to provide Informed Consent<br>• 18 years of age or older<br>• Unilateral user of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K ™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D), including bilaterally implanted subjects that only use one implant in their everyday listening modality<br>• Minimum of 6 months of CI experience<br>• Having used a Naída CI Q70 or a Naída CI Q90 as their primary processor for a minimum of one month<br>• Presently using a current steering strategy<br>• At least moderate open-set speech recognition abilities with implant alone, as defined by achieving a score of ≥ 60% words correct in the AzBio in quiet test using the Naída CI Q90 research processor<br>• English language proficiency as determined by the investigator<br>• Willingness to use a BTE processor for the duration of the study |
| *Inclusion Criteria ARH Cohort* | • Residual low frequency hearing sensitivity (pure tone average of < 70 dB HL for 125, 250, and 500 Hz) and a severe-to-profound high-frequency sensorineural hearing loss (pure tone average of ≥ 70 dB HL for 1,000, 2,000, 3000, 4,000, and 8,000 Hz) in the implanted ear<br>• Willingness to use an in-canal acoustic earhook for the duration of the study |
| *Inclusion Criteria EO Cohort* | • Severe-to-profound sensorineural hearing loss in the low (pure tone average of ≥ 70 dB HL for 125, 250, and 500 Hz) and high frequencies (pure tone average ≥ 70 dB HL for 1,000, 2,000, 3000, 4,000, and 8,000 Hz) in the implanted |

| | |
|---|---|
| | ear |
| *Exclusion Criteria All Cohorts* | • Unrealistic expectations regarding potential benefits, risks and limitations of the investigational device as determined by the investigator<br>• Unwillingness or physical / cognitive inability of subject to comply with all investigational requirements as determined by the investigator |
| *Primary Efficacy Objective* | The primary efficacy objective is to demonstrate that speech recognition in quiet with AutoSense on a M90 processor is no worse than speech recognition in quiet with currently approved software on a Q90 processor. |
| *Secondary Efficacy Objective(s)* | The secondary efficacy objectives are<br>• To demonstrate that speech recognition in noise with AutoSense on a M90 processor is no worse than speech recognition in noise with currently approved software on a Q90 processor.<br>• To demonstrate increased speech recognition in noise with the M90 sound processor when comparing "Omnidirectional" program to AutoSense |
| *Safety Objective* | The primary safety objective is to evaluate whether there are adverse events related to the use of AutoSense on a M90 processor that impact device safety. |
| *Primary Efficacy Endpoint* | AzBio sentence scores in quiet at Baseline with AutoSense on a M90 processor as compared to AzBio sentence scores in quiet at Baseline with currently approved software on a Q90 processor |
| *Secondary Efficacy Endpoint(s)* | • AzBio sentence scores in noise at Baseline with AutoSense on a M90 processor as compared to AzBio sentence scores in noise at Baseline with currently approved software on a Q90 processor.<br>• AzBio sentence scores in noise at Baseline with AutoSense on a M90 processor as compared to AzBio sentence scores in noise at Baseline with a manual "Omnidirectional" program on a M90 processor. |
| *Safety Endpoint* | Absence of unanticipated adverse device effects related to use of AutoSense on a M90 processor |
| *Supporting Data* | Analysis of non-standardized subject questionnaire after two weeks of use of AutoSense OS and a M90 processor in everyday listening situations. |
| *Study Monitoring* | Advanced Bionics, LLC<br>28515 Westinghouse Place<br>Valencia, CA 91355<br>[redacted] |

## 2.0 Glossary

| | |
|---|---|
| ARH | Aidable Residual Hearing |
| AutoSense OS | AutoSense OS 3.0 is a digital signal processing platform that coordinates the settings of device features of the Naída CI M90 processor, also referenced as AutoSense. |
| AutoSound | Implemented on the Naída CI Q90 processor, AutoSound adapts to the listening environment |
| BTE | Behind-the-ear |
| Clinicians Programming Interface (CPI-3) | Interface for cochlear implant sound processor fitting and programming |
| EO | Electric Only |
| Everyday Program | A subjects most used program, typically found in slot 1 of their commercial processor |
| 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 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. |
| Naída CI M90 | Investigational sound processor, also abbreviated as “M90 processor”. [redacted] |
| Naída CI Q90 | Currently approved sound processor used as comparator, also abbreviated as “Q90 processor” |
| NoahLink | Wireless interface for cochlear implant sound processor fitting and programming |
| ListPlayer | Listplayer 3.0 is a proprietary, validated Advanced Bionics software used for speech performance testing |
| SNHL | Sensorineural hearing loss |
| Sound Processor | The external part of a cochlear implant system that captures sound and converts it to digital information |
| SoundWave™ Professional Suite | Commercially available fitting software platform for Naída CI Q90 fitting and programming |
| Target CI | Investigational fitting software platform for Naída CI M90 fitting and programming. [redacted] |
| Verified Everyday Program | Subjects Everyday Program transferred to a Naída CI Q90 research processor with speech levels and settings verified to be appropriate for everyday use. |

# 3.0 Purpose of the Investigation

Advanced Bionics (AB) is introducing AutoSense OS, a digital signal processing platform that coordinates the settings of device features that are designed to maintain speech access and listening comfort in noisy environments. Specifically, AutoSense classifies the acoustic environment during daily life to automatically activate or deactivate sound cleaning features, such as directional microphones and noise management. AutoSense is being implemented on the next generation M90 sound processor. The M90 sound processor is compatible with AB's existing implants (Clarion CII and newer) and sound processing strategies. Target CI, a new fitting software for the M90 sound processor, will be the first version of Advanced Bionics fitting software to use the Phonak Target fitting software architecture.

The overall goal of this clinical study is to demonstrate the safety and efficacy of AutoSense on a M90 processor in users of the HiResolution Bionic Ear System. Hearing outcomes are expected to be similar with AutoSense on a M90 processor as compared to the currently approved software and processors. Therefore, the study described herein uses a non-inferiority design to determine whether sentence recognition in quiet and in noise is no worse with AutoSense on a M90 processor than with currently approved software on a Q90 processor.

# 4.0 Device Description(s)

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 that are already implanted with a HiResolution Bionic Ear System (HiRes 90K, HiRes 90K Advantage, HiRes Ultra or HiRes Ultra 3D).

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

### *4.1.1 AutoSense OS*

AutoSense builds on existing technology, like the front-end processing (FEP) features and microphone directionality (beamforming) in the Naída CI sound processor family.
The front-end processing (FEP) features implemented in AutoSense are mostly based on sound cleaning features on Advanced Bionics' existing Naída sound processor. In addition, two new sound cleaning features (NoiseBlock, WhistleBlock) are being implemented for use with the Acoustic Earhook, and two additional beamformers have been introduced, a static beamformer and "Real Ear Sound".

| Feature | Description |
|---|---|
| **SoundRelax** | Algorithm intended to reduce discomfort with loud transient sounds |
| **WindBlock** | Algorithm Intended to reduce discomfort in windy situations |
| **EchoBlock** | Intended to reduce discomfort in reverberant environments |
| **NoiseBlock** | Intended to reduce steady-state noise on the acoustic signal; [redacted] |
| **WhistleBlock** | Feedback cancellation algorithm to suppress acoustic feedback in the acoustic mode; [redacted] |
| **UltraZoom** | Automatic beamformer |

| Feature | Description |
|---|---|
| Real Ear Sound | [redacted] |
| UltraZoom + SNR boost | |

Table 1: Feature Descriptions

The AutoSound feature in the Q90 sound processor uses an acoustic scene classifier [redacted] The use of a multi-feature set enables the classifier algorithm to determine other scene types such as music, noise- alone, speech in quiet, and speech-in-noise. [redacted] The AutoSense scene types include Clean Speech, Speech in Noise, Speech in Loud Noise, Speech in Car, Comfort in Noise, Comfort in Echo, and Music.

AutoSense is designed to analyze the sound scene and apply the appropriate settings, thereby removing the need for the recipient to manually switch between programs. The microphone directionality is applied independently of the FEPs. As is the case with currently approved technology, all FEP features are applied prior to the electrical signal processing, and therefore the current safety limits on charge balance and current density are maintained.

AutoSense is implemented with default settings that can be modified as needed by the audiologist during the fitting. When operating in the combined electric and acoustic mode, WhistleBlock and NoiseBlock algorithms are available in addition to the other features.

[redacted]

#### *4.1.2 Target CI Fitting Software*

A research version of the Target CI fitting software will be used for the programming of electric and combined electric and acoustic modes of the M90 processor and to adjust the FEP features prior to downloading to the processor. This software is functionally similar to the current approved SoundWave fitting software, providing utilities for changes in stimulation and fitting parameters. The 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 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 and create manual programs.

### 4.2 Investigational Hardware

#### *4.2.1 M90 Processor Package*

The M90 processor is a behind-the-ear (BTE) sound processor based on the Phonak Marvel hearing aid platform. The processor is available in electric-only mode as well as in combined electric-acoustic mode with acoustic earhook, which uses an acoustic receiver that sits in the ear canal. This receiver is also used in commercially-available Phonak hearing instruments.

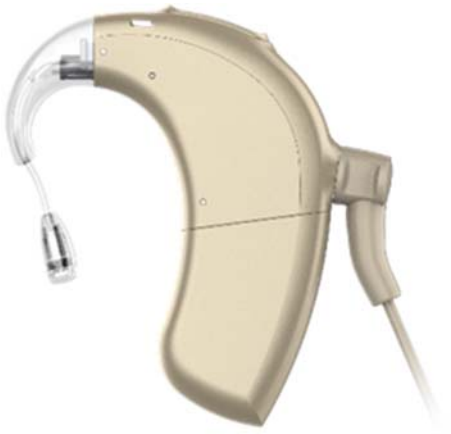

Figure 1. Naída CI M90 Sound Processor

Batteries, battery chargers, T-mics, acoustic earhooks and CPI connecting cable for the M90 processor are all investigational parts of the M90 processor package.

## 5.0 Study Objectives

The primary objective of the proposed clinical study is to demonstrate that speech recognition in quiet with AutoSense on a M90 processor is no worse than speech recognition in quiet with currently approved software on a Q90 processor. Other objectives include speech recognition outcomes in noise.

### 5.1 Study Duration

Each participant fitted with the investigational device in this study is followed for two weeks after the initial fitting with the investigational device.

# 6.0 Study Protocol

## 6.1 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 performance testing will be used to evaluate AutoSense programmed on a M90 processor using Target CI fitting software (investigational device) as compared to approved software on a Q90 processor using SoundWave fitting software (control device). In addition, speech performance will be tested with a manual "Omnidirectional" program on a M90 processor. Statistical analyses will be used to determine if sentence perception with the investigational device is no worse than with the control device, confirmation of the non-inferiority hypothesis. A chronic exposure period of two weeks 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.

## 6.2 Study Endpoints

### *6.2.1 Efficacy*

The purpose of the proposed study is to evaluate efficacy objectives. Speech performance 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 on a M90 processor as compared to AzBio sentence scores in quiet at Baseline with currently approved software on a Q90 processor. Secondary endpoints include:

- AzBio sentence scores in noise at Baseline with AutoSense on a M90 processor as compared to AzBio sentence scores in noise at Baseline with currently approved software on a Q90 processor.
- AzBio sentence scores in noise at Baseline with AutoSense on a M90 processor as compared to AzBio sentence scores in noise at Baseline with a manual "Omnidirectional" program on a M90 processor.

### *6.2.2 Safety*

Adverse event data will be collected and evaluated during the study to ensure that the safety of patients is maintained as per requirements of an IDE and respective center Institutional Review Board guidelines for reporting. The primary safety endpoint is the absence of unanticipated adverse device effects related to use of AutoSense on a M90 processor.

## 6.3 General Subject Population

Advanced Bionics expects to fit up to 24 adult HiResolution Bionic Ear system users with the investigational device in this clinical study across up to 6 study sites in the United States. 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. Depending on the outcome of their audiogram, eligible subjects will be enrolled in one of two cohorts: either an electric only (EO) cohort or an aidable residual hearing (ARH) cohort.

## 6.4 Inclusion and Exclusion Criteria

### *6.4.1 General Inclusion Criteria*

- Ability to provide Informed Consent
- 18 years of age or older
- Unilateral user of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D), including bilaterally implanted subjects that only use one implant in their everyday listening modality
- Minimum of 6 months of CI experience
- Having used a Naída CI Q70 or a Naída CI Q90 as their primary processor for a minimum of one month
- Presently using a current steering strategy
- At least moderate open-set speech recognition abilities with implant alone, as defined by achieving a score of ≥ 60% words correct in the AzBio in quiet test using the Naída CI Q90 research processor
- English language proficiency as determined by the investigator
- Willingness to use a BTE processor for the duration of the study

### *6.4.2 Inclusion Criteria ARH Cohort:*

- Residual low frequency hearing sensitivity (pure tone average of < 70 dB HL for 125, 250, and 500 Hz) and a severe-to-profound high-frequency sensorineural hearing loss (pure tone average of ≥ 70 dB HL for 1,000, 2,000, 3000, 4,000, and 8,000 Hz) in the implanted ear
- Willingness to use an in-canal acoustic earhook for the duration of the study

### *6.4.3 Inclusion Criteria EO Cohort:*

- Severe-to-profound sensorineural hearing loss in the low (pure tone average of ≥ 70 dB HL for 125, 250, and 500 Hz) and high frequencies (pure tone average ≥ 70 dB HL for 1,000, 2,000, 3000, 4,000, and 8,000 Hz) in the implanted ear

### *6.4.4 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

## 6.5 Participant Withdrawal

Study participants may withdraw from the study at any time, with or without reason, and without prejudice to further treatment. The study site Investigator(s) and/or study Sponsor 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

Participants who withdraw or who are discontinued from the study will be reported accordingly to the Institutional Review Board. If a subject was discontinued because of a device-related adverse event or serious adverse event (SAE), the subject must be followed until the 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 capturing system the disposition of each enrolled subject (e.g. completed study, withdrew, discontinued).

# 7.0 Study Procedures

## 7.1 Subject Enrollment

Subjects will be recruited at the participating study centers. Each study center will enroll no more than 1/3 of the subject population for the study. Subjects' willingness and ability to meet the study requirements will be determined and informed consent will be obtained before any study-specific tests or procedures are conducted. A signed and dated informed consent will be kept in the subject's study record with a copy provided to the subject. Study subjects must also sign a release that authorizes access of medical records to the study sponsor, investigators, monitors and the FDA prior to proceeding with study assessments. This release may be contained within the Informed Consent Form (see Appendix B for template) or may be a separate authorization, consistent with institutional policy.

An individual is considered to be enrolled as a study participant once the informed consent document has been signed and dated. Each subject will be assigned a unique identifier at the time of enrollment.

## 7.2 Procedures

Audiometric testing and speech perception testing will be conducted in a single- or double-walled sound booth. Audiometers will conform to ANSI standards for pure-tone and speech audiometry and/or Manufacturer Specifications.

Audiometric testing is performed at the Baseline visit to determine eligibility and assignment to the two cohorts. The AzBio Sentence test in quiet and in noise will be used as the test metric to determine primary and secondary endpoints, respectively. In addition, subjects will complete a sponsor developed subjective questionnaire at the baseline visit and at the end of the two week chronic evaluation period.

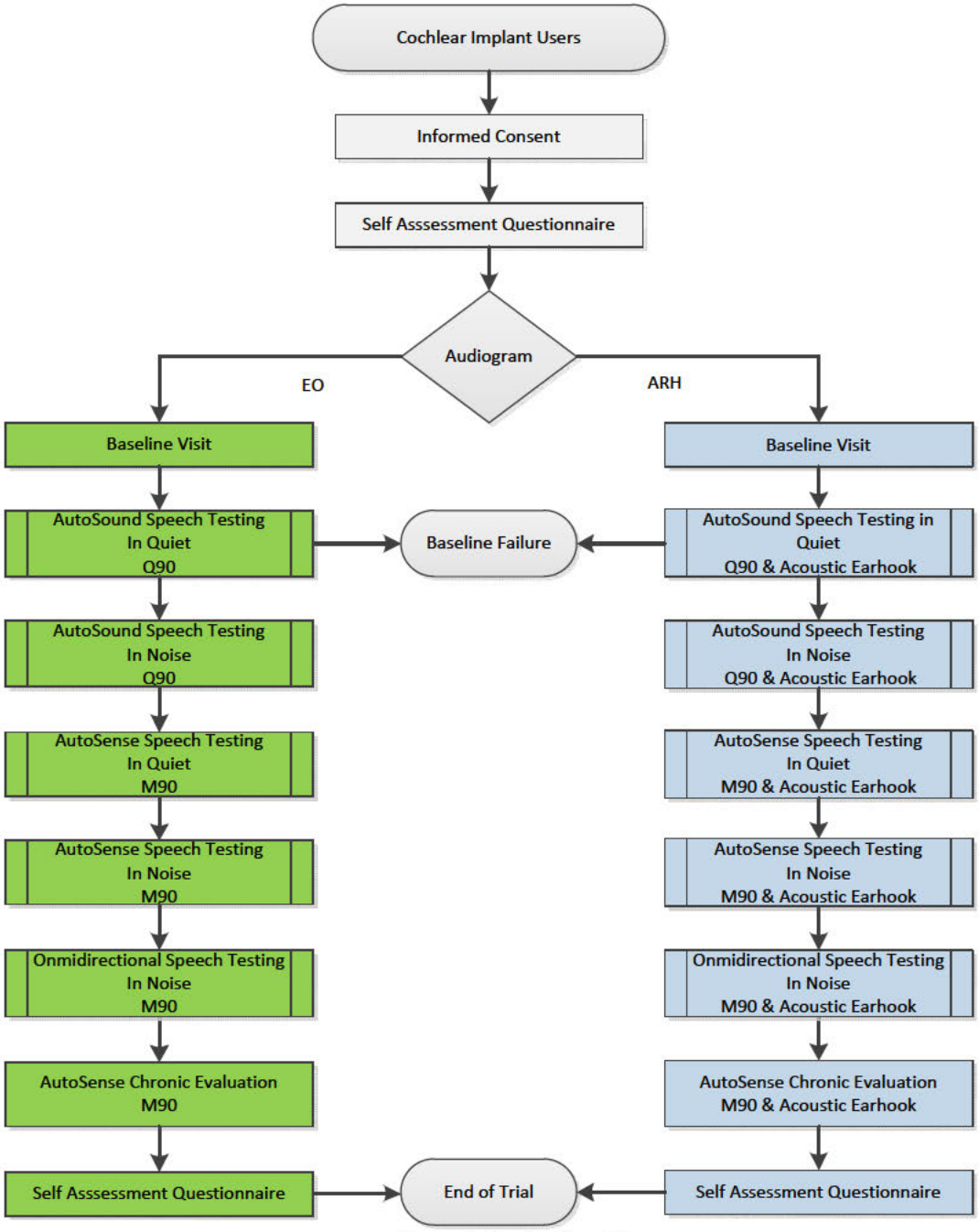


Figure 2. Study Flow Chart

# 8.0 Study Visits

## 8.1 Baseline Visit

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

The following test measures will be administered at the Baseline Visit:

### *8.1.1 Baseline Self-Assessment Questionnaire*

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

### *8.1.2 Audiometric Testing & Cohort Assignment*

Standard audiometric practice, including clinical masking, are applied for the testing, as necessary. Unaided air conduction thresholds using insert earphones at octave frequencies will be obtained for the implanted ear at the following frequencies: 125, 250, 500, 1000, 2000, 3000, 4000 and 8000 Hz.
Subjects will be assigned to one of the two cohorts based on the results of the audiometric testing.

### *8.1.3 Naída CI Q90 Fitting*

After assignment to a cohort, subjects will be fitted with a Q90 research processor with a T-mic (EO cohort) or an acoustic earhook with a dome (ARH cohort) using SoundWave™ Professional Suite version 3.2 and the Clinicians Programming Interface (CPI-3). M and T levels, IDR, as well as ClearVoice and SoftVoice settings will be transferred from the subject's Everyday Program on his/her own sound processor to the research processor. Slight adjustments may be made to M and T levels, as needed. This will be considered the Verified Everyday Program.
For the EO cohort, the Q90 research processor will be programmed to have the T-mic selected. For the ARH cohort, the Q90 research processor will be programmed with the Acoustic Mode set to "On." For both cohorts, the microphone mode will be set to auto UltraZoom, SoundRelax as well as WindBlock will be enabled. This program will be considered the AutoSound program.

### *8.1.4 Naída CI Q90 Speech Perception Testing*

The AzBio Sentence Test (Spahr and Dorman, 2004) is a validated test of open-set sentence recognition ability. The test is scored as total number of words correct which is expressed for results/reporting as percentage correct. The sentence test tokens include both male and female speakers.

Speech stimuli will be administered via an audiometer in combination with ListPlayer, a proprietary software developed by Advanced Bionics.

All speech perception testing will be conducted in a soundfield via calibrated loudspeakers approximately at a distance of one meter from the subject. Speech perception testing in quiet will be performed with a single loudspeaker at 0° azimuth. Speech perception testing in noise will be performed with speech presented from a loudspeaker at 0° azimuth and noise presented from a loudspeaker at 180° azimuth. Testing will be performed unilaterally with the implanted ear. Devices will be removed from the non-test ear (if necessary) and foam plugs will be used to isolate the test ear.

#### *8.1.4.1 AzBio Sentence Testing in Quiet – AutoSound on the Q90 processor*

AzBio Sentence Test in quiet will be administered at 65 dBA at 0° azimuth using the AutoSound program on the Q90 research processor. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

#### *8.1.4.2 Moderate Open-Set Speech Recognition Criteria*

Subjects who do not meet at least moderate open-set speech recognition criteria with the implant alone as defined by a minimum score of 60% in the Naída CI Q90 AzBio Sentence Testing in Quiet will be considered baseline failures and will be exited from the study.

#### *8.1.4.3 AzBio Sentence Testing in Noise – AutoSound on the Q90 processor*

The AzBio Sentence Test in noise will be administered at 65 dBA + 5 dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth using the AutoSound program on the Q90 research processor. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

### *8.1.5 Naída CI M90 Fitting*

Subjects will be fitted with a M90 investigational processor with a M90 T-mic (EO cohort) or a M90 acoustic earhook with a dome (ARH cohort) using the investigational Target CI software wirelessly through NoahLink or with the Clinicians Programming Interface (CPI-3). Strategy, M and T levels, IDR, ClearVoice, SoftVoice and filter settings will be the same as on the Q90 research processor, within the constraints of the fitting software. AutoSense presets in the automatic program will remain unchanged from the pre-defined settings for the AutoSense testing. For the ARH cohort, the M90 research processor will be programmed to have the processor microphone selected. Acoustic and electric cutoff frequencies for subjects in the ARH cohort should approximate those from Q90 research processor. If a match is not available in Target CI, a similar and subjectively acceptable cutoff frequency should be chosen. In addition, a manual "Omnidirectional" program will be created using the "Calm Situation" scene with the Omni microphone mode and the applicable FEPs at the "OFF" settings [redacted].

### *8.1.6 AutoSense Speech Perception Testing*

#### *8.1.6.1 AzBio Sentence Testing in Quiet – AutoSense on the M90 processor*

The AzBio Sentence Test in quiet will be administered at 65 dBA at 0° azimuth using the AutoSense automatic program. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

#### *8.1.6.2 AzBio Sentence Testing in Noise – AutoSense on the M90 processor*

The AzBio Sentence Test in noise will be administered at 65 dBA + 5 dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth using the AutoSense automatic program. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

### *8.1.7 "Omnidirectional" Speech Perception Testing*

The AzBio Sentence Test in noise will be administered at 65 dBA + 5 dB SNR Multi-Talker-Babble (MTB) with speech presented at 0° azimuth and noise presented at 180° azimuth using the "Omnidirectional" manual program. Two lists will be presented and the total number of words per list and words correct will be recorded for each list.

#### *8.1.8 Adverse Event Assessment*

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

## 8.2 Chronic Period

#### *8.2.1 Chronic Period Instructions*

Prior to starting the chronic period, the "Omnidirectional" program will be deleted from the M90 processor and subjects will exclusively use AutoSense on the investigational M90 processor with a T-mic (EO cohort) or an acoustic earhook with a dome (ARH cohort) for 14-21 days during their everyday activities. Slight adjustments may be made to the programing, as needed.

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

#### *8.2.2 Follow-Up Self-Assessment Questionnaire*

Subjects will complete a custom 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 together with the investigational device.

#### *8.2.3 Adverse Event Assessment:*

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

#### *8.2.4 Device Return*

Subjects will be provided a FEDEX envelope and airbill at the baseline visit and will return the investigational M90 processor after 14 to 21 days of chronic use.

### 8.3 Summary of Visit Activities

| Procedure | | Baseline Visit: EO Cohort | Baseline Visit: ARH Cohort | Chronic Period: All Cohorts |
|---|---|---|---|---|
| Informed Consent | | ✔ | ✔ | |
| Demographics & Audiological History | | ✔ | ✔ | |
| Audiometric Thresholds | | ✔ | ✔ | |
| Confirmation of Eligibility | | ✔ | ✔ | |
| Custom Self-Assessment Questionnaire | | ✔ | ✔ | ✔ |
| AutoSound on the Q90 Processor | AzBio in Quiet | ✔ | ✔ | |
| | AzBio in Noise | ✔ | ✔ | |
| AutoSense on the M90 Processor | AzBio in Quiet | ✔ | ✔ | |
| | AzBio in Noise | ✔ | ✔ | |
| "Omnidirectional" program on the M90 Processor | AzBio in Noise | ✔ | ✔ | |
| Adverse Event Assessment | | ✔ | ✔ | ✔ |
| Device Accountability | | ✔ | ✔ | ✔ |

## 9.0 Statistical Methods and Sample Size

### 9.1 General Considerations

The two cohorts to be separately evaluated are the Electric Only (EO) cohort (n=12 pairs) and the Aidable Residual Hearing (ARH) cohort (n=12 pairs). The sample size includes an allowance for dropouts.

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

- Speech recognition in quiet (primary efficacy endpoint) for the investigational AutoSense on a M90 processor vs. AutoSound on the Q90 processor (control).
- Speech recognition in noise (secondary efficacy endpoint) with AutoSense on a M90 processor vs. AutoSound on a Q90 processor.

- Increased speech recognition in noise (secondary efficacy endpoint) with a M90 sound processor when comparing the manual "Omnidirectional" program to AutoSense.
- Subjective feedback (subjective endpoint) about the use of AutoSense on a M90 processor in everyday listening situations.

Descriptive statistics will consist of counts, means, and standard deviations for quantitative variables (primary and secondary outcome measures) and frequency and percent relative frequency for categorical variables.

### *9.1.1 Data Analyses*

#### *9.1.1.1 Efficacy Endpoints*

The primary efficacy endpoint is speech recognition on AzBio in quiet mode for AutoSense on the M90 processor vs AutoSound on the Q90 processor. Non-inferiority analyses will be based on paired t-tests looking at the differences in scores calculated using the Experimental results minus the Control scores at the baseline visit. A one-sided hypothesis test will be used with 0.05 $\alpha$ for the primary efficacy evaluation evaluating the following hypothesis:

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

where $\mu_\Delta$ is the mean of the difference (AutoSense on M90 – AutoSound on Q90) on the AzBio sentence test in quiet. 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 are greater than -0.1 (-10%) for AzBio in quiet mode, which will support that the Investigational condition is non-inferior to the Control condition.

The primary and secondary efficacy endpoints will be first considered for non-inferiority and then for superiority. The superiority tests are penalty-free since the alternative hypothesis for superiority is nested within the alternative hypothesis for non-inferiority. The superiority test will use one-sided p=0.025.

Additional analyses will be conducted to assess any differences based on age of onset or duration of sensorineural hearing loss (SNHL). An analysis of variance (ANOVA) will be used to model the paired differences (Investigational – Control) of AzBio sentences in quiet age of onset and duration of SNHL as the covariate. The analysis will be repeated for AzBio sentences in noise as well as for sentence recognition. The results will also be presented by age of onset and duration of SNHL.

Because the study includes a single visit followed by a chronic period with a subjective questionnaire, the possibility exists that some study participants will not complete the entire test protocol. Given the study design, no data will be imputed but efficacy analysis for other primary and secondary effectiveness endpoints will be repeated for the subset with missing data. In addition, to accommodate potential losses, additional subjects will be enrolled beyond the required sample size per cohort. Efficacy data will not be combined across cohorts.

#### 9.1.1.2 *Type 1 Error Control*

The study will have one primary and two secondary efficacy endpoints per cohort. The Type 1 error needs to be preserved for the two cohorts and three primary and secondary efficacy endpoints.

To address the two independent cohorts, the usual testing for one cohort would rely on one-sided $\alpha$=0.05 but to independently test each cohort, the $\alpha$ will be set to 0.025 to allow testing to be cohort specific. Then results could be separately tested per cohort which would allow significance claims to be made for only one cohort. Then cohort-specific testing will be justified.

For primary and secondary efficacy endpoint testing per cohort, Type I error will be preserved using hierarchical testing where the primary efficacy endpoint will be tested first and then the two secondary efficacy endpoints will be tested next in the pre-specified order (see Section 6.2.1). Cohort-specific claims will be supported for the ordered testing of primary and secondary efficacy endpoints until statistical significance was no longer reached. Thus, to claim statistical significance for all three endpoints, each would need to reach non-inferiority; the subsequent testing for superiority would be penalty-free so the failure to reach superiority would not stop subsequent endpoints from being declared significant based on non-inferiority.

#### 9.1.1.3 *Analyses of Individual Results*

A critical difference score will be used to determine whether individual subjects demonstrate a significant decrease in performance between the Experimental (AutoSense on M90) and Control (AutoSound on Q90) 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 $\sigma$ 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 $\sigma$ 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. The shift from the baseline assessments will be summarized for both the Experimental and Control results indicating *improved*, the *same*, or *deteriorated*. Further the difference between the two strategies will be evaluated and classified as better for the Experimental strategy, the same for both strategies, or better for the Control strategy. 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 the M90 processor relative to AutoSound on the Q90 processor based upon individual data.

#### *9.1.1.4 Safety Endpoint*

The primary safety objective is to evaluate whether there are adverse events related to use of AutoSense OS or the M90 processor that impact device safety.

#### *9.1.1.5 Supporting Data*

Acceptability questionnaire data will be analyzed descriptively using frequency and percent relative frequency for categorical variables.

### *9.1.2 Sample Size Justification*

A total sample size of 12 subjects per cohort is planned for this study based upon efficacy and safety considerations. Previous cohort-specific data were used to estimate the standard deviations (SD) for the paired M90-Q90 differences. The minimum number of subjects required for the study was calculated based upon the primary efficacy outcome measures. The primary efficacy objective is to demonstrate non-inferiority of AutoSense on the M90 processor compared to AutoSound on the Q90 processor for the AzBio sentence test in quiet mode based on a paired t-test. The primary efficacy analyses will test the null hypothesis that the mean of the paired differences ($\mu_\Delta$) in AzBio sentence scores in quiet mode (AutoSense on M90 – AutoSound on Q90) are less than or equal to -10 percentage points, where:

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

Demonstrating that the mean difference, $\mu_\Delta$, is greater than -10 percentage points for all three test conditions will be considered to have shown that M90 is non-inferior to Q90. For both cohorts, previous data supported 6.24% SD for the primary efficacy endpoint (labelled 1 below) and 6.61% SD for the first secondary efficacy endpoint (labelled 2 below). As shown in Table X below, there is >90% power per cohort and per endpoint (power columns) to rule out a -10% null hypothesis supporting non-inferiority (N-I) for a one-sided 2.5% test with statistical significance (one-sided p=0.025) achieved when <-4.98% and <-4.64% paired mean disadvantages are observed while superiority (reach one-sided p=0.025) would be achieved if >5.02% and >5.32% paired mean advantages are observed. The calculations below are based on 8 complete pairs per cohort; a total of 12 pairs will be enrolled in order to accommodate up to four losses per cohort.

**Table 4: Paired t-tests to reject the null hypotheses for non-inferiority and superiority**

| | Power | | Reach N-I | | Reach Sup | |
|---|---|---|---|---|---|---|
| | **1** | **2** | **1** | **2** | **1** | **2** |
| **Test significance level, $\alpha$** | 0.025 | 0.025 | 0.025 | 0.025 | 0.025 | 0.025 |
| **Null hypothesis mean difference, $\mu_0$** | 0% | 0% | -4.98% | -4.64% | 0% | 0% |
| **Alternative mean difference, $\mu_A$** | -10% | -10% | -10% | -10% | -5.02% | -5.32% |
| **Paired SD, $\sigma$** | 6.24% | 6.61% | 6.24% | 6.61% | 6.24% | 6.61% |
| **Effect size, $\delta = \lvert\mu_A - \mu_0\rvert / \sigma$** | 1.603 | 1.513 | 0.805 | 0.810 | 0.804 | 0.805 |
| **Power (%)** | 94 | 90 | NA | NA | NA | NA |
| **N pairs** | 8 | 8 | 8 | 8 | 8 | 8 |

These calculations are based on the T-distribution non-centrality factor as follows:

$$T_{n,NCF} = \frac{\sqrt{n}(\mu_\Delta - \mu_0)}{\sigma}$$

observed based on the non-centrality factor:

$$Power = T_{n-1}(T_{n-1}^{-1}(0.95), n-1, \delta = T_{n,NCF})$$

The sample size (16) can provide sufficient data for determining the safety and reliability of the new strategy. Based on a sample size of 24, the upper bound of the exact event rate was calculated in order to provide complication rates. If no events are observed in 16 subjects, then 15.3% is the upper bound for a one-sided 95% confidence interval on this event rate. This bound provides assurance that events not observed will appear in less than 17.1% of subjects.

## 10.0 Safety Measures

The primary safety objective is to evaluate whether there are adverse events related to use of AutoSense or the M90 processor that impact device safety.

## 11.0 Adverse Event Reporting and Assessment

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

All device-related and non-device-related adverse events (AEs) will be tracked and reported accordingly throughout the 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)]:

### *11.1.1 Adverse Event Definitions and Classifications*

#### *11.1.1.1 Serious Adverse Event*

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.

#### *11.1.1.2 Adverse Device Effect and Serious Adverse Device Effect*

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.

#### *11.1.1.3 Unanticipated Adverse Device Effect*

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.

### *11.1.2 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 A for all CRFs). Information to be recorded on the CRF should include, but is not limited to:

- Date of onset of the adverse event
- 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.

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 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.

### *11.1.3 Anticipated Adverse Events*

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

- There is a possibility that speech and environmental sounds may sound different or louder than what the subjects are accustomed to hearing or that subjects may not like the sound quality of AutoSense on the M90 processor. This risk occurs with all changes to sound-processing, and subjects should be advised of this possibility. If a subject cannot tolerate using AutoSense on the M90 processor or does not like the sound quality, they can return to using their own processor with their baseline programming. In this event, the subject will be withdrawn from the study.
- Subjects may experience some overly loud sounds that result in discomfort. If such loud sounds occur, they can be stopped immediately by removing the headpiece and/or the entire external device.
- Subjects may experience neural tissue damage in the event of chronic overstimulation.
- There is risk of facial nerve stimulation. This risk can be mitigated through reprogramming of the device.
- Subjects may experience intermittent sound or short-term loss of functionality while wearing the device or while being programmed. The intermittency can be eliminated by changing the headpiece, reprogramming the processor, or exchanging the processor.
- Subjects may have permanent residual acoustic or natural hearing damage due to excessive acoustic power.
- Subjects may experience skin or tissue irritation because of the device materials or the equipment may overheat or otherwise malfunction, causing tissue damage.
- Subjects will be exposed to small parts that pose a choking hazard. Care should be taken to avoid choking and the outcomes of choking, such as endoscopic surgery or death.
- Exposure to electromagnetic emissions from the device (external sound processor, internal device) may adversely interfere with other electronic medical devices
- Subjects should only use accessories compatible or designed for the M90 processor (such as the battery chargers) in order to avoid electronic shock.
- Static electricity can potentially damage sensitive electronic components such as the ones used in the cochlear implant system.

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. In these cases, or at any time, subjects may discontinue use of the loaner M90 study processor, and return to using their own processor and baseline program. If subjects stop using the M90 study 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.

# 12.0 Risk Analysis

## 12.1 Approved products

The HiResolution Bionic Ear System is approved under P960058. The commercially approved custom fitting software, SoundWave™ Professional Suite, and Clinician's Programming Interface (CPI-3) will be used during this study to program the Naída CI Q90 processor. Commercially approved, T-mics and acoustic earhooks will be used in conjunction with the Naída CI Q90 processor. The risks associated with use of the approved products are contained in those products' instructions for use.

## 12.2 Risks related to Investigational Hardware

[redacted] The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk. An excerpt from the report is presented in Appendix A.

## 12.3 Risk related to Investigational Software

[redacted] The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk. An excerpt from the report is presented in Appendix A.

## 12.4 Risks related to Cybersecurity

[redacted] The risk analysis contains the determination that the benefit provided by this use-case outweighs any residual risk. An excerpt from the report is presented in Appendix A.

# 13.0 Ethical and Regulatory Obligations

## 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.

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.

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 Informed Consent

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

Before enrollment, the study will be explained to each prospective study candidate. Candidates will be asked to read the approved informed consent form and given the opportunity to ask questions. Once all questions have been answered and the Investigator is assured that the individual understands the implications of participating in the study, the subject will be asked to sign and date the informed consent form. The Investigator will provide a copy of the 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.

## 13.4 Amendments and Deviations

### *13.4.1 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.

#### *13.4.2 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.

#### *13.4.3 Protocol Deviations*

A protocol deviation refers to a study-related activity that is not in compliance with the approved investigational plan/protocol such as an assessment or part thereof are completed incorrectly or omitted or a participant not returning at a defined study interval. Deviation events are to be reported accordingly on a protocol deviation report form (CRF). 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.

## 14.0 Health Insurance Portability and Accountability Act (HIPAA)

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

## 15.0 Study Audits

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

## 16.0 Documents and Records

### 16.1 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)

## 16.2 Study Documentation/Case Report Forms

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

## 16.3 Device Accountability

Participants will be fitted with AutoSense on the investigational M90 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.

## 16.4 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.

## 16.5 Inspection of Records

In the event of an audit, the Investigator agrees to allow representatives of the study Sponsor, FDA or other regulatory authorities to access all study records. Investigators should notify the study Sponsor promptly if an audit request is received from any regulatory or government

agency. A copy of the audit findings if conducted should be forwarded to the study Sponsor following the conclusion of the visit.

## 17.0 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:

[redacted]

Address:

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

# 18.0 Suspension and Termination

## 18.1 Criteria for Terminating the Study

The study Sponsor, Advanced Bionics, reserves the right to terminate the study at any time. However, this right will be exercised only for valid scientific or business reasons, or because of issues related to protection of research subjects. Investigators and IRBs will be notified in writing in the event of termination. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, provide the reason(s) for the termination or suspension and changes to the study visit schedule, as applicable.

## 18.2 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.

# 19.0 References

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.

# 20.0 Protocol Amendments

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

## 21.0 Study Site and Investigator(s)