Evaluation of Remote Fitting in Adult and Pediatric Users of the HiResolution Bionic Ear System

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Contact information

Sponsor	**Advanced Bionics LLC**
Sponsor Address:	25815 Westinghouse Place Valencia, CA 91355 USA

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1. Synopsis

Study Title	Evaluation of Remote Fitting in Adult and Pediatric Users of the HiResolution Bionic Ear System
Sponsor	Advanced Bionics, LLC
Investigational Devices	Target CI DS fitting software AB Remote DS app Naída CI M DS Sound Processor
Study Design	Prospective within-subjects repeated-measures study
Study Population	17 users 13 years or older implanted with a HiResolution Bionic Ear System Up to 5 subjects will be enrolled in a confirmatory Aidable Residual Hearing (ARH) group and 12 subjects will be enrolled in an Electric Only (EO) cohort.
Inclusion Criteria All Subjects	• Ability to provide Informed Consent/Assent • 13 years of age or older • Unilateral or bilateral user of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D) • Minimum of 6 months of CI experience with a minimum of 1 month experience with a Naída CI or Sky CI sound processor • At least moderate open-set speech recognition abilities (defined as speech in quiet score ≥ 60% as assessed at Visit 1) • Minimum average score ≥ 3 on the Mobile Device Proficiency Questionnaire (MDPQ-16) • English language proficiency as determined by the Investigator • Willingness to use a BTE sound processor for the duration of the study
Inclusion Criteria Specific to ARH Group	• 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 for unilaterally implanted subjects and in both ears for bilaterally implanted subjects • Willingness to use an in-canal acoustic earhook for the duration of the study
Exclusion Criteria All Subjects	• Clinical presentation indicative of potential implanted device malfunction • Unrealistic expectations regarding potential benefits, risks and limitations of the investigational device as determined by the Investigator • Unwillingness or inability of subject to comply with all investigational requirements as determined by the Investigator
Primary Study/ Efficacy Objectives	The primary efficacy objective is to demonstrate that speech recognition in quiet after remote fitting is no worse than speech recognition in quiet after in-office fitting.

Primary Study/Efficacy Endpoints	The primary efficacy endpoint are the chronic remote fitting AzBio sentence scores in quiet at Visit 3 as compared to chronic in-office fitting AzBio sentence scores in quiet at Visit 2.
Safety Objective	The safety objective is absence of unanticipated adverse device effects related to remote fitting.
Supporting Data	• Analysis of subjective outcome measures • Analysis of custom subject remote fitting satisfaction questionnaire • Analysis of custom audiologist remote fitting satisfaction questionnaire • Analysis of subject reimbursement questionnaire • Analysis of acute speech perception data • Analysis of in-office fitting vs remote fitting duration • Analysis of psychophysical data
Study Schedule & Duration	<u>Visit 1:</u> • Informed Consent/Assent • Demographics & Audiological History • Mobile Device Proficiency Questionnaire • Reimbursement Questionnaire • Audiometric Thresholds • Speech in Quiet, Personal Sound Processor • Confirmation of Eligibility • Naída CI M DS Sound Processor In-Office Fitting • Acute Speech in Quiet, Naída CI M DS Sound Processor <u>Visit 2:</u> 2-3 weeks after Visit 1 • Subjective Outcome Measure Questionnaire • Chronic Speech in Quiet, Naída CI M DS Sound Processor • Naída CI M DS Sound Processor Remote Fitting via Smart Phone App • Acute Speech in Quiet, Naída CI M DS Sound Processor • Custom Subject Remote Fitting Satisfaction Questionnaire • Custom Audiologist Remote Fitting Satisfaction Questionnaire <u>Visit 3:</u> 2-3 weeks after Visit 2 • Subjective Outcome Measure Questionnaire • Chronic Speech in Quiet, Naída CI M DS Sound Processor

2. Glossary and Abbreviations

AB Remote app	Commercially available mobile application
AB Remote DS app	Investigational research version of the AB Remote app
ADE	Adverse Device Effect
AE	Adverse Event
ARH	Aidable Residual Hearing
BTE	Behind-the-ear
CIP	Clinical Investigation Plan
CRF	Case Report Forms
dB	Decibel
eCRF	Electronic Case Report Forms
EDC	Electronic Data Capture
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.
Hz	Hertz
ICF	Informed Consent Form
IRB	Institutional Review Board
ListPlayer	ListPlayer 3.0 is a proprietary, validated Advanced Bionics software used for speech performance testing
MDPQ-16	Mobile Device Proficiency Questionnaire Short Form
Naída CI M DS	Investigational sound processor used for remote fitting
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
Sound Processor	The external part of a cochlear implant system that captures sound and converts it to digital information
SPL	Sound Pressure Level
Target CI	Commercially available fitting software
Target CI DS	Investigational research version of Target CI fitting software
UADE	Unanticipated Adverse Device Effect

3. Background and Purpose of the Investigation

Advanced Bionics is introducing a remote fitting option to enable audiologists to perform follow-up fittings for unilateral or bilateral CI recipients with or without acoustic earhook. This option is intended to be used for recipients of the HiResolution Bionic Ear System 13 years or older. The remote fitting option will allow the audiologist to connect to the subject's sound processor via a smartphone app.

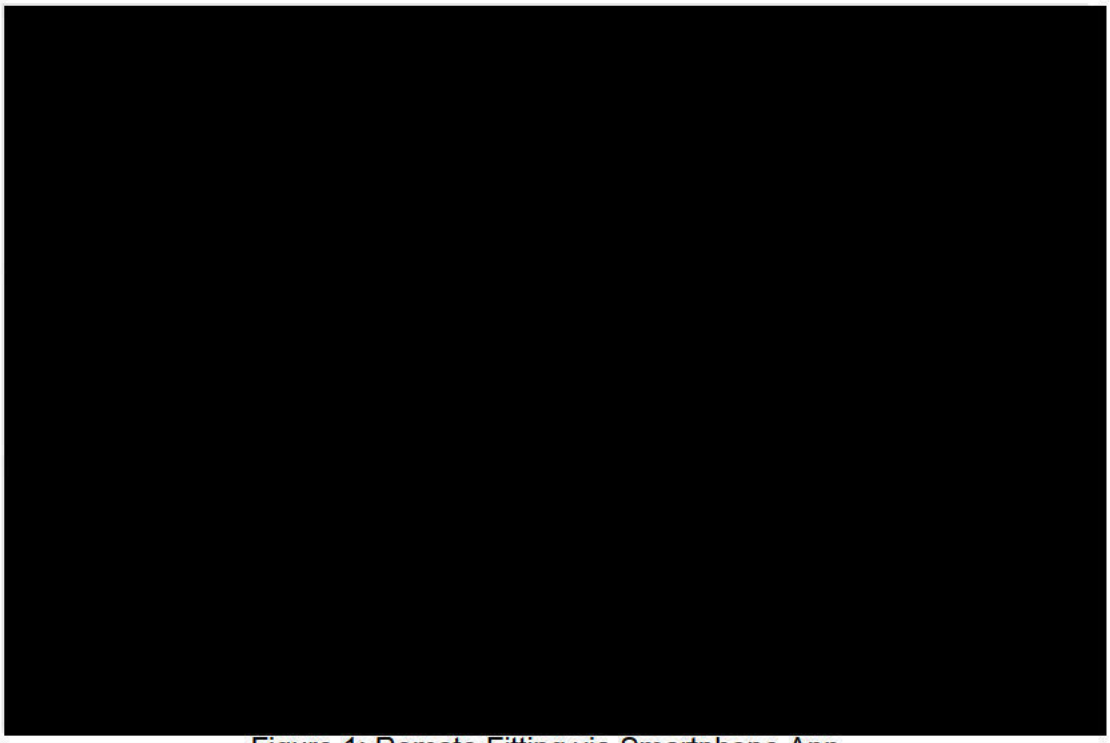


Figure 1: Remote Fitting via Smartphone App

The overall goal of this clinical study is to demonstrate the safety and efficacy of the remote fitting option. Hearing outcomes are expected to be similar whether a study subject's sound processor is programmed in the traditional method in the audiologist's office or whether programming is performed via remote fitting. Therefore, the study described herein uses a non-inferiority design to determine whether sentence recognition in quiet is no worse with remote fitting than in an in-office setting.

4. Investigational Device Description

Investigators participating in this study will be trained audiologists familiar with standard audiological procedures and commercial Target CI fitting software. Investigators will be trained by qualified Advanced Bionics staff on the investigational software and study specific procedures prior to enrollment of the first subject. Each subject will be exposed to the investigational software during the fitting sessions and to the programs created on the Naída CI M DS sound processors with the investigational for the duration of the study.

Commercially approved accessories (acoustic earhooks, T-mics, processor batteries, battery chargers, etc.) will be used during the study.

4.1 Target CI DS Fitting Software

Study sites will be provided with a study laptop containing the Target CI DS fitting software to be used for the remote and in-office programming of electric and combined electric and acoustic modes of the Naída CI M DS sound processors. This software is functionally similar to the currently approved Target CI fitting software, providing utilities for changes in stimulation and fitting parameters. [redacted] All subjects enrolled at a participating study site will be fitted with the same study laptop.

4.2 AB Remote DS App

Study sites will be provided with a smartphone containing the AB Remote DS app to be used for the remote programming of electric and combined electric and acoustic modes of Naída CI M DS sound processors. This software is functionally similar to the current

approved AB Remote app, providing additional utilities for an audiologist to change stimulation and fitting parameters through the app. [redacted] All subjects enrolled at a participating study site will be fitted with the same smartphone.

4.3 Naída CI M DS Sound Processors

The study uses investigational Naída CI M sound processors [redacted]

5. Study Design and Justification

This pivotal 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. Speech performance testing will be used to evaluate remote fitting of Naída CI M DS sound processors (investigational) as compared to in-office fitting of Naída CI M DS sound processors (control). Chronic exposure periods of 2-3 weeks between study visits will be used to evaluate the remote fitting in the subjects everyday hearing environment.

The study is designed as a multi-center study at up to 5 US centers to provide a more representative sample of the target population and make it easier to generalize the findings of the study. In addition, the 2-3 week chronic period between the in-office and remote fittings minimizes the possibility of a carry-over effect between fittings. The study will be considered completed when the last subject has completed their last visit.

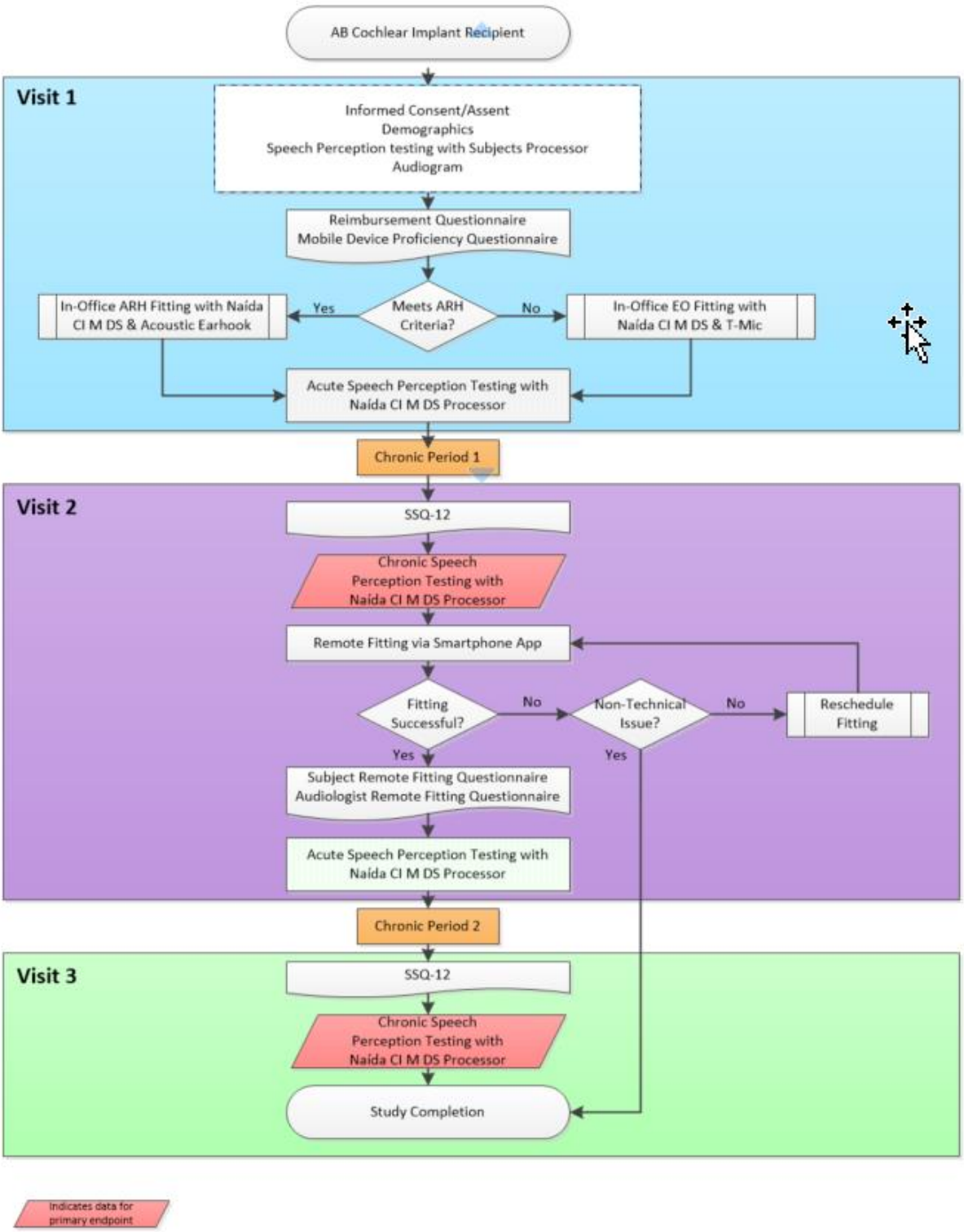


Figure 2: Study Workflow

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. Objectives

The primary efficacy objective is to demonstrate non-inferiority of speech recognition in quiet after remote fitting as compared to speech recognition in quiet after in-office fitting.

7. Study Protocol

7.1 Subject Population and Selection Criteria

Advanced Bionics expects to fit up to 17 HiResolution Bionic Ear system users 13 years or older via remote fitting in this clinical study across up to 5 study sites in the United States. This study population is expected to be representative of the target population for remote fitting. 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 more than 17 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 for aidable residual hearing (ARH) fitting with an acoustic earhook. Unilaterally implanted subjects not meeting ARH fitting criteria will be enrolled for electric only (EO) fitting. Bilaterally implanted subjects meeting ARH criteria only in one ear will be screen failed.

Enrollment in the study is expected to occur over a period of approximately 6 months. Subjects meeting inclusion criteria will participate in 3 study visits over approximately 4-6 weeks.

7.1.1 Inclusion Criteria All Subjects

- Ability to provide Informed Consent/Assent
- 13 years of age or older
- Unilateral or bilateral user of a HiResolution™ Bionic Ear System (HiRes 90K™, HiRes 90K™ Advantage, HiRes™ Ultra, HiRes™ Ultra 3D)
- Minimum of 6 months of CI experience with a minimum of 1 month experience with a Naída CI or Sky CI sound processor
- At least moderate open-set speech recognition abilities (defined as speech in quiet score ≥ 60% as assessed at Visit 1)
- Minimum average score ≥ 3 on the Mobile Device Proficiency Questionnaire (MDPQ-16)
- English language proficiency as determined by the Investigator
- Willingness to use a BTE sound processor for the duration of the study

7.1.2 Inclusion Criteria Specific to ARH Group

- 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 for unilaterally implanted subjects and in both ears for bilaterally implanted subjects
- Willingness to use an in-canal acoustic earhook for the duration of the study

7.1.3 Exclusion Criteria All Subjects

- Clinical presentation indicative of potential device malfunction

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

7.2 Study Endpoints

7.2.1 Efficacy

The purpose of the proposed study is to evaluate speech performance efficacy objectives. The primary efficacy endpoints are chronic remote fitting AzBio sentence scores in quiet at Visit 3 as compared to chronic in-office AzBio sentence scores in quiet at Visit 2.

7.2.2 Supporting data

In addition to acute speech performance, psychophysical data and fitting durations, information from subjective questionnaires will be collected as supporting data:

- Information regarding study participants experience during fitting sessions will be collected via a Subject Remote Fitting Satisfaction Questionnaire.
- Information regarding study participants listening experience during the chronic periods will be collected via a SSQ-12 questionnaire.
- Information regarding study participants reimbursement situation will be collected via a Reimbursement Questionnaire.
- Information regarding investigators' experience during fitting sessions will be collected via an Audiologist Remote Fitting Satisfaction Questionnaire.
- Information regarding acute speech perception will be collected in form of AzBio sentence scores collected immediately after in-office and remote fitting, respectively.
- Information regarding duration of in-office and remote fitting durations will be collected during the fitting sessions.
- Information regarding psychophysical data will be collected during the fitting sessions.

7.2.3 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 remote fitting.

7.3 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.

7.3.1 Audiometric Measures:

Unaided air conduction hearing thresholds (in dB HL) will be measured for the implanted ear(s) using the centers calibrated audiometer and standard audiometric technique for pure-tone air conduction testing.

Unaided air conduction thresholds using insert earphones at octave and inter-octave frequencies will be obtained (125, 250, 500, 1000, 2000, 3000, 4000 and 8000 Hz).

7.3.2 Speech Perception Measures:

All speech perception testing will be conducted using recorded stimuli presented from a single loudspeaker in, at a minimum, a single-walled sound booth capable of accommodating the calibrated speaker orientation. Soundfield levels will be calibrated to 74 dB SPL using a microphone placed at the approximate position of the subject's head (one meter from loudspeaker).

Speech perception measures in the soundfield are to be administered unilaterally for unilaterally implanted subjects and bilaterally for bilaterally implanted subjects via a loudspeaker at 0° azimuth at a distance of one meter from the subject. Speech signals will be presented at 60 dBA.
Devices will be removed from the non-test ear (if necessary) for unilaterally implanted subjects and foam plugs will be used to isolate the test ear for unilateral users.

7.3.3 AzBio Sentence Test

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). 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.
Acute AzBio sentence testing will be performed immediately following in-office and remote fitting sessions, respectively. Chronic AzBio sentence testing will performed at the beginning of each follow-up visit.

7.3.4 Questionnaires

Subjects will be completing a Mobile Device Proficiency Questionnaire (MDPQ-16), subjective outcome measures questionnaires (SSQ-12), a reimbursement questionnaire and a custom remote fitting satisfaction questionnaire. In addition, audiologists will be completing a custom remote fitting satisfaction questionnaire. Questionnaires may be completed on paper or electronically in the EDC system.

7.4 Study Visits and Visit Windows

7.4.1 Schedule of Events

Procedure	Visit 1	Visit 2	Visit 3
Informed Consent/Assent	✔		
Demographics & Audiological History	✔		
Mobile Device Proficiency Questionnaire	✔		
Reimbursement Questionnaire	✔		
Audiometric Thresholds	✔		
AzBio in Quiet, Personal Sound Processor	✔		
Confirmation of Eligibility	✔		
Naída CI M DS Sound Processor In-Office Fitting	✔		
Naída CI M DS Sound Processor Remote Fitting via Smart Phone App		✔	
Acute AzBio in Quiet, Naída CI M DS Sound Processor	✔	✔	
Chronic AzBio in Quiet, Naída CI M DS Sound Processor		✔	✔
Subjective Outcome Measure Questionnaire (SSQ-12)		✔	✔
Custom Subject Remote Fitting Satisfaction Questionnaire		✔ [&]	
Custom Audiologist Remote Fitting Satisfaction Questionnaire		✔ [&]	
Adverse Event Assessment	✔	✔	✔
Device Accountability	✔	✔	✔

[&] Only if remote fitting was successfully completed

7.4.2 Visit 1

This visit is performed at the audiologist's office.

- After informed consent/assent, subject's demographics and hearing history will be captured.
- Subjects' technical competency will be determined using the Mobile Device Proficiency (MDPQ-16) questionnaire and subjects will complete a Reimbursement Questionnaire.
- Speech perception in quiet will be tested using the subject's personal sound processor to determine eligibility for the study.
- Audiometric thresholds are used to determine whether subjects are considered to have aidable residual hearing (ARH). Subjects not meeting the ARH criteria will be fitted under the electric-only criteria (EO). Audiometric thresholds will be determined for the implanted ear only for unilaterally implanted subjects and for both ears individually for bilaterally implanted subjects.
    - Bilateral subjects meeting the ARH inclusion criteria in both ears will be enrolled in the ARH group. Bilateral subjects meeting ARH criteria in only one ear will be screen failed.
- Subjects who meet inclusion and do not meet exclusion criteria are then fit with a Naída CI M DS sound processor in the audiologist's office. Unilateral ARH subjects will be fitted with an acoustic earhook and EO subjects will be fitted with a T-mic. Bilateral subjects meeting the ARH criteria will be fitted with an acoustic earhook in both ears. Fitting parameters on the Naída CI M DS sound processor should mimic the parameters on the subject's personal sound processor as closely as possible and be adjusted for comfort and sound quality as needed. Program settings will include two programs, one AutoSense OS program with and a second manually selected Calm situation program. This will be considered the in-office fitting.
- Acute speech perception in quiet is performed to confirm the in-office fitting on the Naída CI M DS sound processor.
- Adverse events and device observations are collected, as needed, and device accountability is performed.
- Following the visit, the subject will test the Naída CI M DS sound processor chronically for 2-3 weeks during their day-to-day activities.

7.4.3 Visit 2

Visit 2 will occur 2-3 weeks after Visit 1.

- The visit will start at the audiologist's office with subjects completing a subjective outcome measures questionnaire.
- Chronic speech perception in quiet will be tested using AzBio sentences.
- In addition, the audiologist will introduce the remote fitting application to the subject and will pair the smartphone with the subject's Naída CI M DS sound processor. For the purposes of the study, a dedicated fitting smartphone will be used that is only used for remote fitting.
- The subject will then move to the remote fitting location. The audiologist will initiate the remote fitting session through Target CI DS, and the subject will open the application on the remote fitting smartphone. Both parties will engage verbally to ensure audibility and visualization via smartphone video during the call. The audiologist then remotely connects to the subject's sound processor to begin the fitting session. The fitting will include measurement of impedances, measurement of electrode-specific neural response imaging (NRI), programming of M levels, and live speech stimulation to confirm acceptability of adjustments. Fittings for AHR subjects will include a review of acoustic and electric cutoff frequencies and gains at 65 dB. Additional adjustments may be made as needed to ensure comfort and clarity of the Map and to ensure acceptability of the fitting

during the subject's chronic wear period. The audiologist and subject will then confirm the completion of the fitting and both parties close their respective remote fitting session applications.

- Should technical issues occur during the remote fitting session, the audiologist will first try to mitigate the issues, for example by instructing the subject to turn off their outgoing video or to move to a different location in case of poor connection.
- The audiologist will re-schedule the remote fitting session should the remote app fitting not be completed because technical issues could not be mitigated during the session. Adverse events and/or device observations are collected and device accountability is performed, as needed.
- If remote fitting cannot be completed due to non-technical reasons (e.g. subject was not able to sufficiently communicate with the audiologist via the app), the subject will be exited from the study. Reasons for non-completion of the remote fitting will be documented. Adverse events and/or device observations are collected and device accountability is performed.

- After the remote fitting session is successfully completed, the subject will rejoin the audiologist in person for acute speech perception in quiet to confirm the remote fitting on the Naída CI M DS sound processor.
- In addition, the audiologist and the subject each will complete a custom remote fitting satisfaction questionnaire.
- Adverse events and device observations are collected and device accountability is performed, as needed.
- Following the visit, the subject will test the remotely-fitted Naída CI M DS sound processor chronically for 2-3 weeks during their day-to-day activities.

7.4.4 Visit 3

Visit 3 will occur 2-3 weeks after the Visit 2.

- This visit is performed at the audiologist's office and begins with subjects completing a subjective outcome measures questionnaire.
- In addition, chronic speech perception in quiet will be tested.
- Adverse events and device observations are collected, as needed, and device accountability is performed.
- The subject will then return the Naída CI M DS sound processor and return to using their personal sound processor. Standard clinical follow-up is recommended after subjects exit the study.

7.5 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 M DS 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. Statistics

Data from all subjects meeting inclusion and not meeting exclusion criteria will be combined across all sites for the analysis. No study center will enroll no more than 1/3 of the total subject population for the study. The sample size includes an allowance for dropouts.

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

- Chronic speech recognition in quiet (primary efficacy endpoint) for the investigational remote fitting vs. in-office fitting (control).
- Acute speech recognition in quiet for remote fitting vs. in-office fitting (supporting data).
- Subjective feedback (supporting data) about subject reimbursement, subjective outcome measures and remote fitting satisfaction.
- Fitting duration for remote fitting vs. in-office fitting (supporting data).
- Psychophysical data for remote fitting vs. in-office fitting (supporting data).

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

While baseline variables like age at time of implant, duration of severe-to-profound hearing loss at time of implant, and duration of cochlear implant use at time of enrollment have been shown to be correlated with speech perception results in other studies (Rubinstein et al., 1999; Tyler and Summerfield, 1996), these variables are not expected to affect the outcome of this clinical investigation due to the within-subject design of the study.

The sections below provide a high-level overview, more detailed descriptions will be included in the statistical analysis plan for the study. The statistical analysis plan will be finalized prior to analysis of the data to avoid bias from post-hoc definitions. Deviations from the statistical analysis plan will be documented and included in the clinical study report.

8.1 Sample Size Justification

The primary efficacy endpoint is speech recognition on AzBio in quiet mode for remote fitting (Investigational) vs. in-office fitting (Control). Non-inferiority analyses will be based on paired t-tests looking at the differences in scores calculated using the Investigational speech scores minus the Control speech scores. A one-sided hypothesis test will be used with 0.025 α for the primary efficacy evaluation evaluating the following hypothesis:

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

where $\mu\Delta$ is the mean of the difference (remote fitting – in-office fitting) 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] In addition, during validation of the AzBio sentence test, Spahr and colleagues showed that the 95% confidence intervals for average speech recognition for two-list administration approximated 10%. Based on these observations, performance falling outside of the sample confidence interval or greater than 10% would be considered a clinically significant difference (Spahr et al., 2012). Statistically significant test results that reject the null hypotheses, indicating that the means of the paired differences are greater

than -10 percentage points for AzBio in quiet mode, which will support that the Investigational condition is non-inferior to the Control condition. Previous data supported 6.24% SD for the primary efficacy endpoint. As shown in Table 1 below, with a sample size of 8 complete pairs there is 97% power to rule out a -10% null hypothesis supporting non-inferiority for a one-sided 2.5% test with statistical significance.

Table 1: Paired t-tests to reject the null hypotheses for non-inferiority and superiority

	Non-Inferiority
Test significance level, α	0.025
1 or 2 sided test?	1
Null hypothesis mean difference, μ_0	-10
Alternative mean difference, μ_A	0
Paired SD, σ	6.24
Effect size, $\delta = \lvert\mu_A - \mu_0\rvert / \sigma$	1.603
Power (%)	97
N	8

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

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

observed based on the non-centrality factor:

$$Power = T_{n-1}\left(T_{n-1}^{-1}(0.975), n-1, \delta = T_{n,NCF}\right)$$

The above sample size calculation provides the minimum sample size for the EO cohort. In addition, 5 ARH subjects will be enrolled in the study to provide confirmatory data for the electric and acoustic fitting mode for subjects wearing an acoustic earhook. The incidence of acoustic earhook use among Advanced Bionics recipients is low, less than 2.5% of US recipients. As such, a confirmatory sample of 5 subjects is considered sufficient in order to provide clinical data via descriptive statistics. Outcomes after remote fitting are expected to be similar between the EO cohort and the ARH group. The total sample size was expanded to 17 (12 EO and 5 ARH) as the expected dropout rate due to withdrawals or lost to follow-up is not expected to exceed 4 subjects. Based on a sample size of 17, the upper bound of the exact event rate was calculated in order to provide complication rates. If no events are observed in 17 subjects, then 16.2% is the upper bound for a one-sided 95% confidence interval on this event rate.

8.2 Data Analyses

Subjects will be analyzed separately for the AzBio in quiet mode for remote fitting (Investigational) and for the in-office fitting (Control) as well as the paired difference. All enrolled subjects that meet the inclusion / exclusion criteria will be included in the intent-to-treat (ITT) population. The analysis will be repeated for the per-protocol (PP) population excluding subjects with major protocol deviations. Protocol deviations will be classified as major if they affect data integrity for the primary endpoint or subject safety as defined in Table 2 below.

Table 2: Major Protocol Deviations

Protocol deviations affecting data integrity of the primary endpoint	Chronic speech perception testing not performed in, at a minimum, a single-walled sound booth.
	Chronic speech perception testing performed without prior calibration of sound field levels to 74dB SPL.
	Chronic speech perception testing not performed at 0° azimuth.
	Chronic speech perception testing not performed at a distance of one meter from the subject.
	Chronic speech perception testing not performed with speech signals presented at 60 dBA.
	Chronic speech perception testing performed without removing hearing devices (if necessary) from contralateral ear for unilaterally implanted subjects.
	Chronic speech perception testing performed without using foam plugs in contralateral ear for unilaterally implanted subjects with residual hearing in the contralateral ear.
	Chronic speech perception testing not performed using two lists of AzBio sentences.
	Chronic speech perception testing not performed bilaterally for bilaterally implanted subjects.
Protocol deviations affecting subject safety	Protocol deviations that result in a serious adverse event

8.2.1 Efficacy Endpoints

The primary efficacy endpoint is chronic speech recognition using AzBio sentence tests in quiet for remote fitting vs. in-office fitting. Non-inferiority analysis will be based on a paired t-tests looking at the mean difference in scores (D) calculated from the chronic remote fitting speech perception testing (investigational) minus the chronic in-office fitting speech perception scores. Unilateral and bilateral involvement will be additionally considered in two separate manners for the primary effectiveness analysis endpoint to assess the remote vs local difference. First, the unilateral and the bilateral subjects will be analyzed as separate subgroups. Second, a linear regression analysis for the paired difference will include a covariate for whether the subject is unilateral (reference group) or bilateral in order to evaluate the laterality effect. Clinical significance is defined as ruling out a -10 percentage point difference by rejecting the null hypotheses, indicating that the means of the paired differences are greater than – 10 percentage points, as evidence that the remote fitting is non-inferior to the in-office fitting.

Because the study includes follow-up visits, the possibility exists that some study participants will not complete the entire test protocol. Multiple imputation will be used to analyze the primary efficacy endpoint (SAS PROC MIANALYZE; Little and Rubin [2002]). Subject values will be imputed using observed test scores and selected baseline variables.

8.2.2 Supporting Data

The following supporting data will also be evaluated using descriptive statistics:

- subjective outcome measures
- custom subject remote fitting satisfaction questionnaire
- custom audiologist remote fitting satisfaction questionnaire
- subject reimbursement questionnaire
- acute speech perception data
- in-office fitting vs remote fitting duration
- psychophysical data
- duration of in-office vs remote fitting.

8.2.3 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 (remote fitting) and Control (in-office fitting) 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 α = 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. The shift 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 remote fitting relative to in-office fitting based upon individual data.

8.2.4 Safety Endpoint

The safety objective is the absence of unanticipated adverse device effects related to remote fitting.

8.2.5 Supporting Data

Subjective outcome measures, remote fitting acceptability questionnaire data, data from reimbursement questionnaires, acute speech perception data, fitting durations and psychophysiological data will be analyzed descriptively. Descriptive statistics will consist of counts, means, and standard deviations for quantitative variables and frequency and percent relative frequency for categorical variables.

Additionally, subject demographics and study results will be presented descriptively to assess site heterogenity.

9. 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)]:

9.1 Adverse Event Definitions and Classifications

9.1.1 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.

9.1.2 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.

9.1.3 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.

9.2 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 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 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.

9.3 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 the study sound processor used in the study. This risk occurs with all changes to sound-processing, and subjects should be advised of this possibility. If a subject cannot tolerate using the study sound processor or does not like the sound quality, they can return to using their own sound 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 sound processor, or exchanging the sound 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 study sound processor (such as the battery chargers) in order to avoid electric 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. 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.

9.4 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.

10. Informed Consent Process

A study site's Informed Consent Form template and Informed Assent 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 informed assent template and assistance in adapting the templates to conform to local requirements (Appendix C). All informed consent and informed assent 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. The process for pediatric subjects is described in section 11.

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 and informed assent forms 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 and informed assent forms 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.

10.1 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.

11. Vulnerable Population

11.1 Pediatric Subjects

HiResolution Bionic Ear System is approved for use in pediatric patients between 12 months and 17 years with profound bilateral sensorineural hearing loss, and in adults 18 years and up with severe to profound bilateral sensorineural hearing loss. Advanced Bionics recognizes that the benefit/risk profiles of remote fitting could be different among patients of different age ranges, especially with regards to pediatric patients at very young ages. Therefore remote fitting is intended to be used in follow-up programming of Advanced Bionics cochlear implant recipients 13 years and older who are able to self-report a preference for different fitting characteristics (e.g., mapping or features). The benefits of remote fitting are the same for pediatric subjects as for adults (see section 12.1). While

audiological care for pediatric patients in this age range is similar to adults, it is still important to ensure that remote fitting is a suitable option for these pediatric age group. Therefore Advanced Bionics is planning to enroll pediatric subjects 13 years of age and older in this study. After informed consent is obtained from a parent / legal guardian, informed assent will be obtained from the pediatric subject. The informed assent process will closely follow the informed consent process for adult subjects.

Governing IRBs will give special consideration to protecting the welfare of vulnerable subjects per federal regulations. The study will only enroll pediatric subjects who have the ability to understand the requirements of the study and who are able to communicate untoward experience or preference for different fitting characteristics, as determined by the Investigator. After exiting the study, pediatric subjects will return to using their personal sound processor and will be followed per standard clinical care.

12. Benefits and Risks

12.1 Benefits

Recipients of the HiResolution Bionic Ear System 13 years and older will significantly benefit from the option of remote fitting in lieu of in-office follow up fitting visits at their center. Many recipients live a considerable distance from their cochlear implant center and traveling to the center for in-office follow-up visits can pose a significant burden. In addition, remote fitting provides recipients who are not able to drive themselves the possibility to connect with their audiologist without having to rely on others for transportation. Remote fitting can also protect vulnerable subjects in cases where in-person contact poses a health risk, for example during a global pandemic. These benefits are expected to outweigh the risks.

12.2 Risk related to Approved Products

[redacted] The risks associated with use of the approved products are contained in those products' instructions for use.

12.3 Risk related to Investigational Hardware

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

12.4 Risk related to 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 presented in Appendix A.

In addition, the following risks are related to remote fitting:

- [redacted]

- [redacted]

13. Suspension or Premature Termination

13.1 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 M DS 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 M DS sound processor until a determination is made whether the study will continue.

13.2 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.

14. Monitoring, Device Accountability and Data Management

14.1 Monitoring Procedures

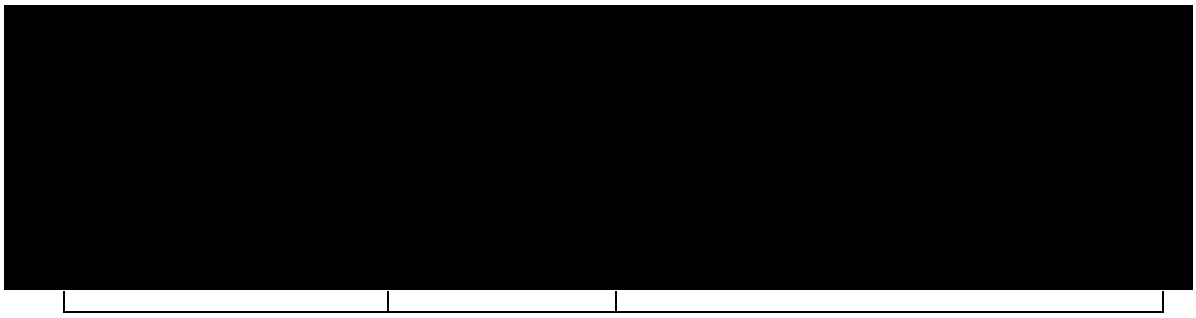
Independent monitoring of the study for clinical protocol compliance will be conducted periodically to oversee compliance with the regulatory and clinical aspects of the study. The Clinical Monitor will maintain current knowledge of the study through observation, review of study records and source documentation,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

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.

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:



Address:

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

14.2 Device Accountability

Participants will be fitted with a Naída CI M DS sound processor at their participating study center. 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 Naída CI M DS sound processors 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 study laptop with the investigational Target CI DS software as well as the smartphones programmed with the investigational remote fitting app.

Advanced Bionics will track all investigational study laptops and smartphones sent to study centers using the manufacturer serial numbers. Study centers will return the investigational devices to Advanced Bionics after all subjects have been exited from the study and Advanced Bionics will track the receipt of those devices.

14.3 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.

15. Statements of Compliance

15.1 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.

15.2 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.

15.3 Documents and Records

15.3.1 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)

15.3.2 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.

15.3.3 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.

15.3.4 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.

15.4 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.

15.5 Study Funding

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

16. Amendments and Deviations

16.1 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, FDA, and the IRB.

16.2 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 in the Electronic Data Capture system. 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.

16.1 Emergency Deviations

Investigators are not allowed to deviate from the protocol, unless required to protect the rights, safety, or well-being of subjects. 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.

17. 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.

18. Bibliography

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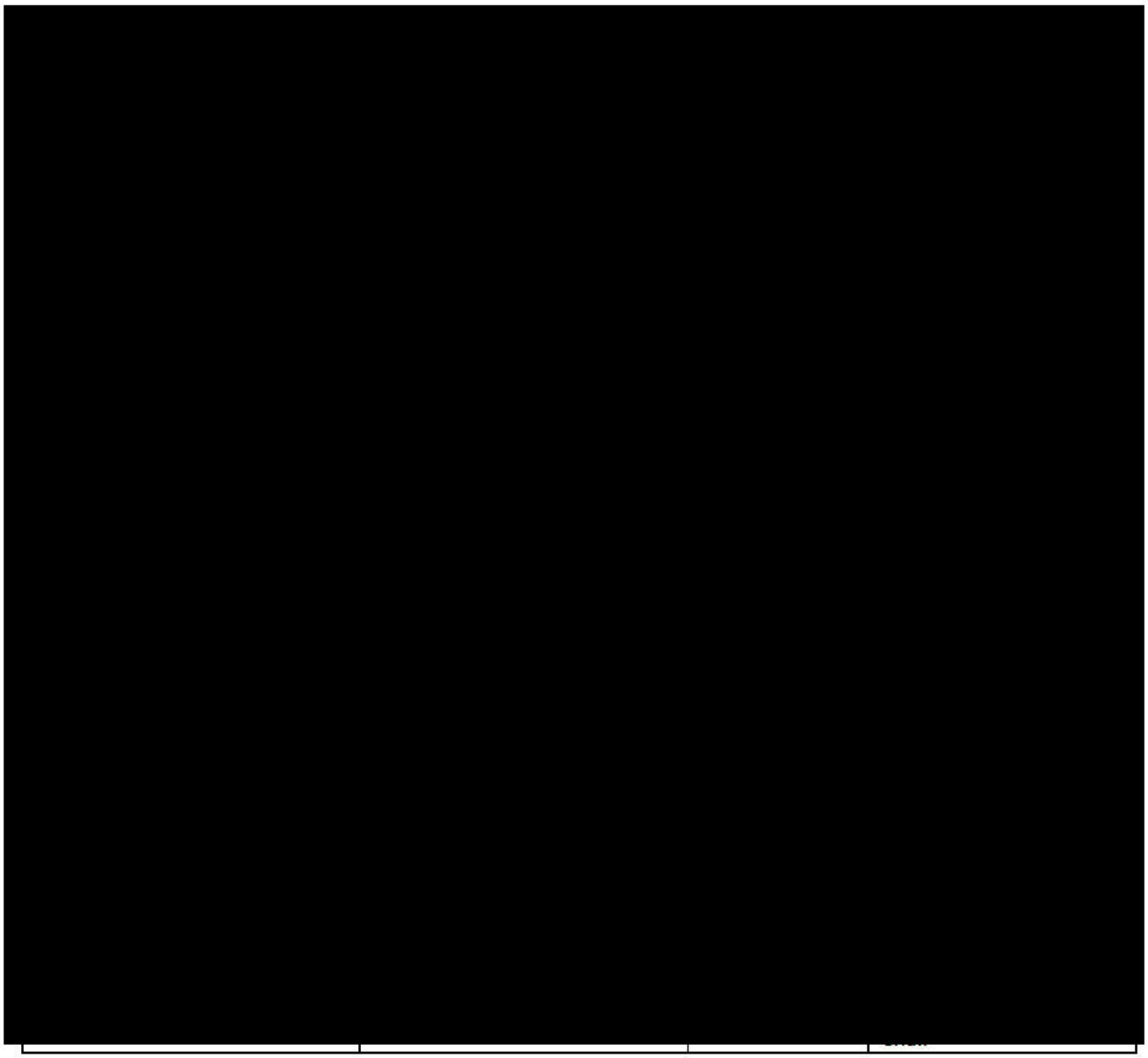
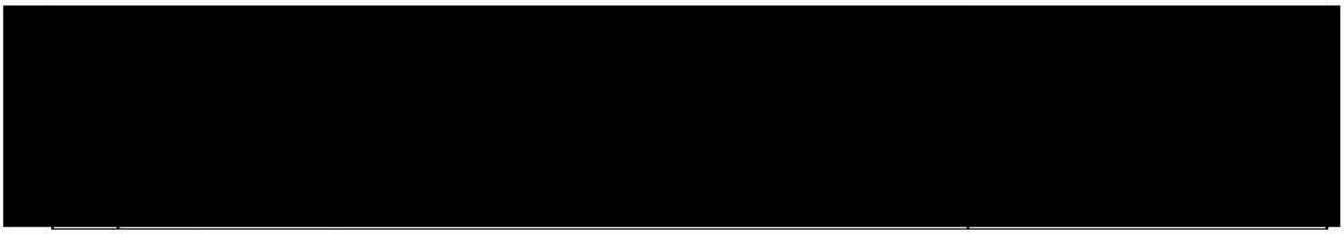
19. Study Sites, Investigators and External Organizations

19.1 Study Sites and Investigators



19.2 External Organizations



20. Revision History (if applicable)

Revision	Summary of Change	Date
1.0	Original Version	03-May-21
1.1	[redacted]	[redacted]
1.2	[redacted]	[redacted]

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

In addition, I assume responsibility for protocol compliance for persons to whom I delegate study related tasks.

Study Center: _____

Principal Investigator Name: _____

Principal Investigator Signature: _____

Signature Date: _____