[redacted]

Non-Significant Risk Study of a Cochlear Implant Headpiece

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1.0 Study Synopsis

Study Title	Non-Significant Risk Study of a Cochlear Implant Headpiece	
Sponsor	[redacted]	
Device	The device being evaluated is a cochlear implant headpiece and compatible selection of magnets of varying strength that allow for head-worn retention to be individualized.	
Study Design	Single-group, prospective, within-subjects, repeated measures, subjective report	
Number of Participants	Between 20 and 200 participants	
Number of Sites	The principal and sub-investigators at Advanced Bionics will oversee study progress. Participants will be consented and engaged at private locations across the United States and Canada by Study Staff.	
	Inclusion Criteria	The following criteria will be used: • Pre- or post-lingually deafened. • Fluent in English, French, Spanish or capable of communication with a caregiver who is providing consent. • Adult or child implanted with a commercially available Advanced Bionics cochlear implant. Children and adult participants are included to ensure device retention is appropriate for all implant populations. • Have (or caregivers have) the cognitive and functional capability to comply with all directions during the study • Be able to remove their own headpiece • Have (or caregivers have) the cognitive and functional capability to complete the questionnaire required for the study • Capable (or caregivers are capable) of reading and understanding patient information materials and giving written informed consent
	Exclusion Criteria	Medical or cognitive conditions that, in the opinion of the investigators and study staff, is likely to interfere with study procedures or likely to confound evaluation of study endpoints.
	Study Objective	The objective of this study is the evaluation of an investigational cochlear implant headpiece for individuals who are current users of FDA approved Advanced Bionics cochlear implants. This investigational headpiece and

	compatible magnet is expected to provide acceptable comfort and retention for existing cochlear implant users. In this study, participants will subjectively report on their experience with the investigational headpiece during daily life.
Efficacy Parameters	Questionnaires: Self report of headpiece retention and comfort
Primary Study Endpoint	Completion of all provided questionnaires that capture subjectively reported headpiece retention and comfort, as compared to baseline.
Primary Safety Endpoint	Cumulative frequency of adverse events and events per participant
Safety Parameters	Rate of adverse events
Control	Each participant will act as their own control
Research Hypothesis	The investigational headpiece and compatible magnets will provide participants with a retention option that is acceptable for daily use.
Study Schedule	Consent: Participants or will sign an informed consent form prior to the conduct of any study procedures. Baseline: Participants will complete a questionnaire regarding experience with their own headpiece at the time of consenting and enrollment. Follow up: Participants will evaluate the investigational headpiece during a chronic period of up to one-year or until the investigational headpiece receives FDA approval. They will complete questionnaires at two-month intervals. Off-Study: Participants will return their investigational headpieces to the Sponsor.
Experimental Hypothesis	A significant portion of study participants will report that the investigational headpiece is acceptable for wear during daily life.

2.0 Identification and description of the investigational device

Cochlear implant device introduction

Each Advanced Bionics cochlear implant system operates with an implantable portion, and external sound processor, and headpiece that acts as a communication link between the implant and sound processor. These devices, including both internal and external components, have been authorized by the FDA and other Regulatory bodies for commercial distribution. As these implant systems have become more widely distributed and technology evolves, increased data and user feedback as well as component obsolescence issues mandate that new designs for external devices be developed for use with existing cochlear implant systems.

Cochlear implant headpieces allow sound processors to transmit audio information and power through a recipient's skin to power the internal implant and supply the audio source that is electrically reproduced for hearing. The headpiece is worn on the head, sitting on the hair or scalp in a position behind and slightly above the ear. The headpiece contains a magnet that is attracted to a second magnet embedded under the skin in the internal implant, the attraction between these two magnets provides retention to the head.

The current, commercially approved, [redacted]addresses clinical needs expressed by customers: retention, irritation, and aesthetics. [redacted]P design allows for user-adjustability of the headpiece magnet strength, allowing up to a maximum of five full-strength magnets to be used with the [redacted] or as few as one magnet. Changing the number of magnets and distance between magnets allows one to change retention strength. Cochlear implant recipients will have different thickness of skin and hair between the case of the implant and the external headpiece; for this reason, there is a need to individualize the selection of magnets to find a retention strength that holds the headpiece in place during daily activities, while remaining comfortable.

Description of the investigational device and design options

- Investigational Headpiece: All investigational headpieces used in this study will use the same electrical components and biocompatible materials as the commercially available, FDA-approved headpieces distributed by Advanced Bionics. The investigational headpieces will have design modifications to molded materials (e.g. plastic, rubber, silicone or Teflon) to address cosmetic issues (e.g. mold flash or mold sink) or design improvements resulting from subject feedback. The investigational headpieces will have possible modifications to the headpiece magnet type/material used. Prior to subject use, the investigational device shall

be subject to stimulation safety and integrity testing, electrical testing, safe temperature profiling and materials biocompatibility testing.

- Implantable Systems: All cochlear implant recipients enrolled in the study will be current users of an FDA approved cochlear implant manufactured by Advanced Bionics.
- External Wearable Cochlear Implant Sound Processors: All Advanced Bionics implantable systems operate in conjunction with a number of externally worn, FDA-approved, sound processors and headpieces. Subjects enrolled in the study will be current users of these commercially available sound processors.
- Directions for Use: Participants who have a cochlear implant will have already been implanted with a device manufactured by Advanced Bionics independently of this study and according to standard medical practice and will be familiar with the usage of their own clinically approved standard devices.

3.0 Design of the clinical investigation

3.1 Study Objective

- The objective of this study is to evaluate an investigational cochlear implant headpiece for individuals who are current users of FDA approved Advanced Bionics cochlear implants. This investigational headpiece and the compatible magnet is expected to provide acceptable comfort and retention for existing cochlear implant users. In this study, participants will subjectively report on their experience with the investigational headpiece during daily life.

3.2 Study Investigators and Study Staff

- The investigational site team for this study consists of clinical, research and field staff employed by the sponsor. At all study activities, at least one Investigator or Study Staff will be available to supervise conduct. All study Investigators and Study Staff will receive training specific to the study protocol and their study responsibilities.

3.3 Management and recruitment of study participants

Recruitment

- Participants who meet the study criteria will be recruited from cochlear implant recipient populations across North America. A participant's willingness and ability to meet the follow-up requirements will be determined and informed consent will be obtained. Participants under the age of 18, will be consented through a parent or guardian and provided a complementary assent, with age specific language for children ages 7-12 years and children ages 13-17 years. A signed and dated copy of this consent will be kept in the participant's study record and copy provided to the participant.

Participant Screening

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

Inclusion criteria for participant selection

- Pre- or post-lingually deafened.
- Fluent in English, French, or Spanish or capable of communication with a caregiver who is providing consent.

- Adult or child implanted with a commercially available Advanced Bionics cochlear implant. Children and adult participants are included to ensure device retention is appropriate for all implant populations.
- Have (or caregivers have) the cognitive and functional capability to comply with all directions during the study
- Be able to remove their own headpiece
- Have (or caregivers have) the cognitive and functional capability to complete the questionnaire required for the study
- Capable (or caregivers are capable) of reading and understanding patient information materials and giving written informed consent

Exclusion criteria for participant selection

- Have any significant medical condition that, in the opinion of any of the investigators, is likely to interfere with study procedures or likely to confound evaluation of study data.

Criteria and procedures for participant withdrawal or discontinuation

- Participants may withdraw from the study at any time, with or without reason, and without affecting continued standard of medical care they would receive. Participants can be discontinued from the study for the following reasons:
    - Withdrawal of consent
    - A safety concern noted by a clinician that endangers the participant or cannot be tolerated for medical and/or ethical reasons
    - Inability of the participant to perform the tasks necessary to provide usable data for the study.
- The Investigator or Study Staff will complete a log to document the disposition of each enrolled participant (completed study, withdrew, discontinued). Any withdrawal or discontinued participation will be documented.

Consent

- Participants should appear to meet all of the eligibility criteria and none of the criteria for ineligibility before they are asked to consent to continue with study-specific screening procedures. Written informed consent must be obtained for all people who are potential study candidates before any study-specific tests or procedures are performed.

- Study candidates who meet general entry criteria will be asked to sign the Institutional Review Board (IRB) approved Informed Consent form before any study-specific tests or procedures are performed. Study personnel should explain that even if a patient agrees to participate in the study and signs an informed consent form, certain diagnostic or screening procedures might demonstrate that the patient is not eligible to continue participation. Examples of situations that may lead to

exclusion from further participation are the presence of exclusionary medical or psychological conditions or a condition that might confound study results.

- Investigators or the Study Staff and the candidate for consent will share English, Spanish, or French language fluency.

- For study activities conducted in the State of California, research subjects will also be provided with the California Experimental Subject's Bill of Rights.

Point of enrollment

- An individual is considered to be enrolled as a study participant only after completion of the informed consent. Each participant will be provided ample time to consider participation in the trial. Once enrolled, the participant will be assigned a unique identifier. [redacted]

Total expected duration of the clinical investigation

- The present study is expected to continue at least for one year from initiation or until the investigational headpiece receives FDA approval, whichever comes last.

Expected duration of participation

- Duration of participation will vary from the time of enrollment to the one-year end point or until the investigational headpiece receives FDA approval, whichever comes last.

Number of participants required to be included in the clinical investigation

- A minimum of 20 participants will be enrolled in this present study, with a maximum of 200 participants.

3.4 Description of all study procedures

The present study uses a single-group, prospective, within-subjects, repeated measures design, participants will complete questionnaires to provide subjectively reported opinions of investigational headpiece retention and comfort. Questionnaires will be available in English, French, and Spanish. English language examples are provided in Appendix 2.

Candidates for study participation and caregivers or family will be referred by audiologists from audiological and medical centers across the United States and Canada. The audiologist will be informed of this study by local Study Staff and the referral will be made through a telephone call, email, or in-person conversation. All participants will be recipients of commercially available Advanced Bionics' cochlear implants and the commercially available sound processors.

Study staff will contact prospective participants through a telephone call, email, or in-person conversation. A private location will be used for all study activities. Examples of private locations include but are not limited to: a meeting room in a hotel, a meeting room in an office building or clinic, or the participants home. Study staff will consent all participants prior to introduction of the cochlear implant headpiece. Participant contact information will be collected at this time, no other identifying or health-related information will be collected. If the participant is too young or unable to provide consent otherwise, a parent or guardian will complete the consenting process and the participant will be asked to assent to study participation.

Following completion of the informed consent, subjects will be asked to fill out a Baseline Questionnaire answering questions about their current headpiece. After completion of Baseline Questionnaire, Study staff will introduce the investigational headpiece and magnets to the participant. Participants and caregivers will have been previously trained and experienced in the use of their existing cochlear implant headpiece. Study staff will select the appropriate investigational headpiece magnet strength, identifying which magnet strength has appropriate retention. Appropriate retention is subjectively defined as retention sufficient to hold the headpiece in place during activities of daily life, while avoiding discomfort.

Following selection of the headpiece magnet and appropriate fit of the investigational headpiece, the study staff will introduce the Investigational Headpiece questionnaires that participants will complete at the initial visit and two-month intervals throughout their participation in the study. Participants will receive a number of questionnaires that would span the study duration. Pre-paid envelops will be provided to allow participants to return completed questionnaires every two-months for the duration of the study.

At any time during the study, participants may request meetings with Investigators or Study Staff for changes in magnet strength or adjustments to the investigational headpiece, these meetings will be coordinated through a telephone call, email, or in-person conversation to set up additional visits.

Participants will return the investigational headpiece to the Sponsor at the end of this study. A pre-paid shipping envelope will be provided for this purpose.

Data collection and analysis of the present study will be administered from the Sponsor's location. Recruitment, participant consenting, and fitting of the investigational cochlear implant headpiece may be completed by study staff, with professional training with the Advanced Bionics cochlear implant system, at locations outside of the Sponsor's location. Investigators and study staff will complete training for this study that includes:

- Good Clinical Practice, including investigator responsibilities
- Informed consent procedures, including requirements for inclusion, exclusion, and all foreseeable risks
- Study protocol and procedures
- Processes for recording and reporting adverse events
- Device accountability procedures
- Data collection and correction procedures, source documentation, and record retention requirements

3.5 Documentation and Records

All study records (e.g., protocol, correspondence with the Sponsor and the IRB, IRB approvals, participant contact information, consent forms, reports) will be maintained by the Principal or Sub-Investigators as long as local document retention regulations require. If an Investigator opts to discontinue participation in the study, all records will be transferred to a mutually agreed designee (i.e., another Investigator).

3.6 Compensation

Compensation for participation in this study will include:

- Travel, Parking, and Mileage will be paid by Advanced Bionics
- Meal expenses for the participant and one additional person will be reimbursed by Advanced Bionics. Reimbursement per-meal may not exceed [redacted].
- Participants will receive [redacted] for participation in this study, with an additional [redacted] for each questionnaire received by the Sponsor.
- Payment of [redacted] will be sent following the first visit and questionnaire payments will be sent semi-annually afterward.

4.0 Device accountability, risks, and benefits

4.1 Anticipated clinical benefits

- Participants are not expected to experience clinical benefits beyond those present during the use of existing headpieces. Some participants may find that this headpiece offers greater retention, as the investigational headpiece design may allow for increased retention. The clinical benefit of this latter case is more consistent headpiece retention.

4.2 Risks associated with participation in the clinical investigation and mitigation

- **Anticipated adverse device effects:** The investigational headpiece has a new bottom profile with respect to the currently approved headpieces. The risks identified below are risks associated with currently FDA-approved headpieces. There are no anticipated new risks associated with the investigational design.

Procedure	Risk	Risk Mitigation
Use of investigational hardware	Wearing the device is uncomfortable, minor skin irritation.	The bottom profile (in contact with patient skin) is functionally similar to previously approved headpiece design.
Use of stronger magnet strength	Skin flap irritation/pain due to excessive pressure. ICS extrusion due to skin flap breakdown.	Ability to add or remove magnets to adjust headpiece strength.
Use of weaker magnet strength	Headpiece falls off patient's head frequently due to insufficient retention force.	Ability to add or remove magnets to adjust headpiece strength

- **Residual risks:** All risk have been reduced as far as possible.
- **Risk mitigation:** The risk controls are located in the table above. Additionally, the subjects will be instructed to discontinue use of the investigational headpiece immediately in the event that any discomfort is encountered. Subjects will always have access to their commercially approved hardware at all times during the study and will continue to use these commercially approved headpieces at the end of the visit.

5.0 Ethical and Regulatory Obligations

5.1 Study Conduct

- The sponsor/investigator agrees 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 the International

Council on Harmonization (ICH) Guidelines, and internal Standard Operating Procedures (SOPs). The sponsor/investigator will conduct all aspects of this study in accordance with all national and local laws of the pertinent regulatory authorities.

- The sponsor/investigator will assure proper implementation and conduct of the study including those duties delegated to other appropriately qualified individuals and Study Staff. The sponsor/investigator and Study Staff will demonstrate due diligence in recruiting and retaining study participants.

5.2 Institutional Review Board and Ethics Committee

- Before initiation of the study, the sponsor/investigator must obtain approval of the research protocol, informed consent form, and any advertisement for subject recruitment, from the governing IRB/IEC complying with the provisions specified in 21 CFR Part 56 and any other applicable regulations. The approval letter must be signed by the IRB chairman or designee, identify the IRB name and address, the clinical protocol by title and/or protocol number, and include the date that approval was granted. The sponsor/investigator is responsible for obtaining continued review of the clinical research at intervals not exceeding one year or as otherwise specified by the IRB.

5.3 Informed Consent

- All informed consent forms and patient information sheets must contain the minimum elements as mandated by FDA (21 CFR Part 50) and ICH guidelines and will be subject to IRB approval.

- Before recruitment and enrollment, each prospective study candidate will be given a full explanation of the study, allowed to read the approved informed consent form, and be provided the opportunity to ask any questions that may arise. Once all questions have been answered and the sponsor/investigator is assured that the individual understands the implications of participating in the study, the subject will be asked to give consent to participate in the study by signing the informed consent form. The sponsor/investigator will provide a copy of the signed informed consent form to each subject.

- If an amendment to the protocol changes the subject participation schedule in scope or activity, or increases the potential risk to the subject, the informed consent form must be revised, submitted to the IRB for review and approval. The revised informed consent form must be used to re-consent a subject currently enrolled in the study if he or she is affected by the amendment. The revised informed consent form must be used to obtain consent from any new subjects who are enrolled into the study after the date of the approval of the amendment.

5.4 Amendments and Deviations

- Protocol Amendments: This protocol is to be followed exactly. Changes to the research covered by this protocol must be implemented by formal protocol amendment. A

formal amendment cannot be initiated until regulatory approval is obtained (if applicable) and it has been reviewed and approved by the IRB.

- Emergency Deviations: Emergency deviations or modifications may be initiated without IRB approval only in cases where change is necessary to eliminate an immediate apparent hazard to subjects. Emergency deviations or modifications must be reported to the IRB no later than 24 hours after the emergency.

- Protocol Deviations: Deviation from the clinical protocol and protocol requirements including ICH/GCP guidelines will be reviewed and evaluated on an ongoing basis, reported to the IRB as necessary and appropriate corrective actions implemented as necessary.

5.5 Health Insurance Portability and Accountability Act (HIPAA)

- All subjects must sign a HIPAA authorization form prior to participation in the study.

5.6 Monitoring of the Study

- A data monitoring committee is not needed for this study as there is no significant risk to participants and the investigation is carried out with a single Principal Investigator.

6.0 Documents and Records

6.1 Pre-Study Documentation Requirements

- Prior to consenting any subjects, the following documents must be available:
    - A copy of this protocol that has been signed and dated by the Principal Investigator and Sub-Investigators
    - A copy of the written IRB approval of the protocol
    - A copy of the written IRB approval of the Informed Consent Form and the approved Informed Consent Form
    - A copy of the curriculum vitae of the Principal Investigator and Sub-Investigators

6.2 Study Documentation

- Study records are comprised of source documents and all other administrative documents.

- 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 is in support of the protocol specifications, e.g., lab reports, clinic notes, subject completed questionnaires, telephone logs, informed consent, etc. All draft, preliminary and pre-

final iterations of a final report are also considered to be source documents, e.g., faxed lab reports and hard copy lab reports, faxed initial results and hard copy final report.

6.3 Device Accountability

- Study equipment will be provided and tracked by Investigators and/or Study Staff.

7.0 Adverse Event Reporting

- All adverse events will be monitored throughout the duration of the study.

7.1 Adverse Events and Adverse Device Effects

An ***adverse event*** (AE) is defined as any undesirable clinical occurrence experienced by a study subject either during or subsequent to the procedure whether or not it is considered to be device-related.[1] The definition of AE also applies to 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 will be reported as an AE. This definition includes events occurring during the follow-up period and ending when the subject completes the final follow-up visit and returns to use of the baseline device.

A ***serious adverse event*** (SAE) is an adverse event that leads to any of the following:

- Death due to any cause
- A life-threatening illness or injury[2]
- A permanent impairment of a body structure or a body function
- Inpatient hospitalization[3], prolongation of hospitalization (extension equal or greater than 24-hours) or surgical intervention to prevent permanent impairment to body structure or body function
- Fetal distress, fetal death, congenital abnormality or birth defect

An ***adverse device effect*** (ADE) is any untoward and unintended response to a medical device.

A ***serious adverse device effect*** is an adverse device effect that resulted in any of the consequences characteristic of a serious adverse event 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.

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[1] Device-related includes any procedure related to the study device inclusive of placebo.
[2] Life-threatening refers to an event in which the subject was at risk of death at the time of the event; not an event which hypothetically, if more severe, would be resultant in death.
[3] Inpatient hospitalization is defined as a hospital admission for a period of greater than 24 hours.

An ***unanticipated adverse device effect*** is any serious adverse effect on: health, safety, or any life threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

All adverse events and adverse device effects, serious and non-serious, will be reported to the Clinical Research Department at Advanced Bionics.

Information to be reported should include, but is not limited to:

- Type/Nature of event
- Date of onset
- Severity
- Duration/rate of resolution
- Course of action taken
- Outcome
- Relationship to investigational materials
- Anticipated or unanticipated
- Other relevant information as necessary

The communication requirements for Adverse Events and Adverse Device Effects are as follows:

Classification	***Type of Communication to AB***	***Communication Time to AB***	***Contact at AB***
Serious Adverse Event Serious Adverse Device Effect Unanticipated Adverse Device Effect	Telephone call and email or FAX notification of adverse event Adverse Event Case Report Form (CRF) with all available information	Within 48 hours of detection	PI
Non-Serious Adverse Event Non-Serious Adverse Device Effect	Adverse Event CRF with all available information	Reviewed at monitoring visits	PI

Evaluation of any serious adverse events (SAE), serious adverse device effects (SADE), and unanticipated adverse device effects (UADE) will be conducted as follows: Confirmed UADEs will be reported to the IRB within 10 days after receiving notice of the event. Reporting for confirmed SAEs and SADEs will be performed in accordance with local IRB reporting requirements. If it is determined that an event or effect presents an unreasonable risk to

subjects, this study, or those parts of the study presenting that risk, will be terminated as soon as possible. Such termination shall occur not later than 5 working days after the determination is made and not later than 15 working days after the Sponsor first received notice of the effect.

7.2 Record Retention

Records of the study (e.g., protocol, correspondence with Sponsor and IRB, IRB approvals, patient records, consents, and reports) must be maintained at least as long as local document retention regulations require.

7.3 Suspension and Termination

- Advanced Bionics reserves the right to terminate the study but intends only to exercise this right for valid scientific or business reasons and reasons related to protection of research subjects. The IRB will be notified in writing in the event of termination.
- Possible reasons for study termination include: The discovery of an unexpected, significant, or unacceptable risk to subjects enrolled in the study.

7.4 Investigator Responsibilities

The sponsor/investigator agrees to the following:

- Agree to sign and adhere to this protocol.
- Be willing to provide a signed a dated copy of the curriculum vitae including a statement of relevant experience including the dates, location, extent, and type of experience.
- Agree to disclose involvement in an investigation or other research that was terminated, and an explanation of the circumstances that led to termination.
- Agree to conduct the investigation in accordance with the investigational plan, all applicable FDA regulations, and conditions of approval imposed by the reviewing IRB.
- Supervise all testing involving human participants.
- Agree to obtain written informed consent before any study specific procedures are performed in accordance with GCP and that the requirements for obtaining informed consent are met.

8.0 World Medical Association Declaration of Helsinki

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI
Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000
Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002
Note of Clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004

INTRODUCTION

The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international

requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

9.0 Basic Principles for all Medical Research

It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

Medical research involving human subjects should only be conducted if the importance of the

objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

The subjects must be volunteers and informed participants in the research project.

The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

Both authors and publishers have ethical obligations. In publication of the results of research, the

investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

10.0Additional Principles for Medical Research Combined with Medical Care

The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.[4]

At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.[5]

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[4] The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or

- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

[5] The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.

The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Somerset-West, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.

11.0 Appendix 2 Questionnaires

AB	Non-Significant Risk Study of a Cochlear Implant Headpiece **Investigational Headpiece Baseline Questionnaire**	[redacted]

Subject ID: ☐☐☐ - ☐☐☐ Subject # - Subject Initials (First, Middle, Last; if no middle initial, use a "-")	***Visit Date:*** ☐☐ - ☐☐ - ☐☐☐☐ Month Day Year

If you have any questions during the evaluation, please consult with the [redacted]

Please indicate your rating:

1. Rate the **retention** of your personal headpiece				
Very Acceptable	Acceptable	No Opinion	Unacceptable	Very Unacceptable
☐	☐	☐	☐	☐

2. Rate the **comfort** of your personal headpiece				
Very Acceptable	Acceptable	No Opinion	Unacceptable	Very Unacceptable
☐	☐	☐	☐	☐

Thank you for you participation.

	Non-Significant Risk Study of a Cochlear Implant Headpiece **Investigational Headpiece Fitting Form**	[redacted]

Subject ID: ☐☐☐-☐☐☐ Subject # - Subject initials (First, Middle, Last; if no middle initial, use a "-")	***Visit Date:*** ☐☐-☐☐-☐☐☐☐ Month Day Year

To be completed by Study Staff:

Right Side	N/A ☐	Headpiece SN:
[redacted]		

Left Side	N/A ☐	Headpiece SN:
[redacted]		

Study Staff (Print Name)	
Signature:	
Date:	

	Non-Significant Risk Study of a Cochlear Implant Headpiece **Investigational Headpiece Questionnaire**	[redacted]

Subject ID: ☐☐☐ - ☐☐☐ Subject # - Subject initials (First, Middle, Last; if no middle initial, use a "-")	***Visit Date:*** ☐☐ - ☐☐ - ☐☐☐☐ Month Day Year

Please refer to the following instructions during your time wearing the new headpiece.

1. Provide feedback on the headpiece and magnet configurations when requested.
2. If any headpiece discomfort arises during the study, please discontinue use of the investigational headpiece and resume use of your personal headpiece.
3. Return all investigational products to the Advanced Bionics Study Staff after the evaluation.

If you have any questions, please consult with the [redacted]

Date questionnaire was completed: ☐☐ - ☐☐ - ☐☐☐☐

Month Day Year

Please rate:

1. Is **retention** of the investigational headpiece acceptable?				
Very Acceptable	Acceptable	No Opinion	Unacceptable	Very Unacceptable
☐	☐	☐	☐	☐

2. Is **comfort** of the investigational headpiece acceptable?				
Very Acceptable	Acceptable	No Opinion	Unacceptable	Very Unacceptable
☐	☐	☐	☐	☐

Thank you for you participation.