Esteem® Totally Implantable Hearing System

Post Approval Study
New Subject Enrollment

Protocol Number 0205

June 14, 2010
November 15, 2010
January 05, 2016
August 20, 2019

CONFIDENTIAL **DO NOT COPY**

THIS PROTOCOL CONTAINS CONFIDENTIAL INFORMATION FOR USE BY THE INVESTIGATORS AND THEIR DESIGNATED REPRESENTATIVES PARTICIPATING IN THE EVALUATION OF THE *ESTEEM® SYSTEM.* IT SHOULD BE HELD CONFIDENTIAL AND MAINTAINED IN A SECURE LOCATION. IT SHOULD NOT BE COPIED OR MADE AVAILABLE FOR REVIEW BY ANY UNAUTHORIZED PERSON OR FIRM.

TABLE OF CONTENTS

PROTOCOL SUMMARY

Title: *Esteem*® Totally Implantable Hearing System Post-Approval Study

Purpose: To evaluate the safety and efficacy of the *Esteem*® Totally Implantable Hearing System (hereafter called the *Esteem*® *System*) implanted by newly-trained surgeons in subjects suffering from moderate to severe hearing loss.

Trial Design: The Post-Approval Study is similar to the PMA pivotal clinical trial, which was designed as a prospective, multi-center, non-randomized, clinical trial to evaluate the safety and efficacy of the *Esteem*® *System*. For this trial the subject acts as his or her own control.

This trial has been designed to meet the United States' regulatory requirements.

Enrollment Size: A minimum total of 45 new subjects will be enrolled and implanted in this study, with the requirement of 45 evaluable subjects for analysis of efficacy endpoints. For safety endpoints, a minimum of 109 evaluable subjects will be required.

Subject Population: Subjects 18 years of age and older who have moderate to severe sensorineural hearing loss (HL) defined by PTA, have a healthy middle ear, have an unaided speech discrimination score of equal to or better than 40%, and have previously worn a hearing aid for a minimum of 30 days are eligible for inclusion in the Post Approval Study. See detailed inclusion/exclusion criteria for specifics.

Questions: The following questions are to be answered:

- Is the *Esteem*® effective through 1 year follow-up?
- Is the *Esteem*® safe through 1 year follow-up?
- Is the incidence of facial pareses/paralysis at 1 month follow-up no greater than 7%?

Primary Objectives:

1. To demonstrate that the *Esteem® System* improves the speech threshold of sensitivity for hearing and identifying speech signals as well as or better than the pre-implant hearing aid (aided condition).

   Endpoint: Comparison of the speech reception threshold (SRT) using the *Esteem® System* as compared to the pre-implant aided condition.

2. To demonstrate that the *Esteem® System* is as effective as or better than the hearing aid for improving speech discrimination (intelligibility) as shown by the word recognition score at 50 dB.

   Endpoint: Comparison of the word recognition score using the *Esteem®* compared to the pre-implant aided condition.

3. To determine the incidence of Serious Adverse Device Effects (SADE) and Adverse Device Effects (ADE) and the incidence rate of device failures and replacements.

   Endpoint: The analysis of the incidence of SADEs and device failures and replacements at each follow-up.

4. To demonstrate that the incidence of facial pareses/paralysis is no greater than the 7% incidence experienced in the PMA clinical trial.

   Endpoint: The analysis of the incidence of facial pareses/paralysis at 1 month follow-up.

5. To demonstrate that the subjects' cochlear function remains unchanged with the *Esteem® System* as shown by comparison of the subjects' pre-implant baseline bone conduction threshold versus the subjects' post-activation visit bone conduction threshold.

   Endpoint: Comparison of bone conduction threshold (BC) using forehead placement post activation compared to the pre-implant BC threshold.

Secondary Objectives:

1. To show that the *Esteem® System* improves Quality-of-Life when compared to the baseline aided condition as shown by APHAB results.
2. To gather subject feedback and comments on the use of the *Esteem® System* relative to the pre-implant hearing aid (aided condition) as shown by the *Esteem®* Questionnaire.

Sponsor Contact Information:

Envoy Medical Corporation, Inc. (EMC)
4875 White Bear Parkway
White Bear Lake, MN 55110
Tel: (651) 361-8000
Customer Service Fax: (651) 361-8099
www.envoymedical.com

Changes in Revision 04

Change footer revision number from Rev 03 to Rev 04
Clarify the enrollment totals for efficacy and safety endpoints in Protocol Summary, sections 1.4, 2.2 and 4.7
Change sponsor address of Envoy Medical Corporation to current address
Miscellaneous typo corrections

1 INTRODUCTION

1.1 Device Name

The device being evaluated in this Post Approval Study is the *Esteem*® Totally Implantable Hearing System (*Esteem*® *System*). The *Esteem*® has recently been approved by FDA for the US market under PMA P090018. This study fulfills the requirement for one of the Post Approval Studies.

1.2 Device Description and Principle of Operation

The *Esteem*® *System* is a totally implantable hearing system designed to improve hearing in subjects suffering from moderate to severe hearing loss that is sensorineural in origin.

The *Esteem*® *System* consists of three components that are implanted in the subject: A Sound Processor (SP) is implanted under the scalp over the temporal bone and is connected via leads to two piezoelectric transducers (called the Driver and Sensor), which are implanted in the middle ear. In addition there are two components that will be used during the implant of the *Esteem*® *System*: An intra-operative test system, and the *Esteem*® programmer. The *Esteem*® programmer will also be used by the audiologist for follow-up *Esteem*® *System* management. When the *Esteem*® *System* is activated the subject will receive an additional external component, the Personal Programmer. See full description below.

The *Esteem*® *System* works in the following manner: The Sensor is placed on the incus bone. This Sensor senses mechanical vibrations transmitted from the eardrum through the malleus and/or incus bone, then converts these vibrations into an electrical signal, which is sent to the SP. The SP amplifies and filters the signal, then sends it to the Driver, which has been attached to the head of the stapes. The Driver converts the modified electrical signal back to mechanical vibrations that is transferred to the stapes. The stapes bone vibrates the oval window, which produces pressure waves in the fluid of the cochlea. The cochlea converts the pressure waves to nerve impulses, which are transmitted via the eight cranial nerves to the brain, where they are interpreted as sound.

Prior to implantation of the Driver and Sensor, the incus will be separated from the stapes at the incudostapedial joint and 1 to 3 mm will be resected from the long process of the incus. This will allow the Driver to be placed directly over the stapes bone and prevent feedback to the Sensor that could result in poor system performance.

The *Esteem*® programmer enables the physician and/or the audiologist to program each subject's implanted SP to that subject's specific audiological need. The programmer is also used to interrogate the *Esteem*® *System's* Sound Processor and provides the physician and/or the audiologist with diagnostic capabilities both during the operative procedure and during follow-up clinic visits.

The Personal Programmer enables the subject to select from three (3) pre-set programs for background noise levels, to place the device on standby, and to increase or decrease the volume of his/her *Esteem*® *System* SP using radio frequency (RF) telemetry. The Personal Programmer is battery operated and has a low battery indicator.

The Envoy Medical Intra-operative System Analyzer (ISA) is used during the implant procedure to verify that the Sensor and Driver are positioned correctly. It will also be used at the end of the implant procedure to verify that the *Esteem*® *System* is functioning appropriately.

1.2.1 Anticipated Changes in Device

There are no plans to change the device or the protocol during this Post Approval Study.

1.3 Indications for Use

The *Esteem*® is intended to alleviate hearing loss in patients by replicating the ossicular chain and providing additional gain. The *Esteem*® is indicated for patients with hearing loss that meet the following criteria:

- 18 years of age and older
- Stable bilateral sensorineural hearing loss
- Moderate to severe sensorineural hearing loss as defined by Pure Tone Average (PTA)
- Unaided Speech discrimination scores greater than or equal to 40%
- Normally functioning Eustachian tube
- Normal middle ear anatomy
- Normal Tympanic Membrane
- Adequate space for *Esteem*® implant determined via a high resolution CT scan
- Minimum of 30 days of experience with appropriately fit hearing aids

1.4 Justification for the Investigation

In order to study the safety and effectiveness of the *Esteem*® *System* in a clinical environment, a post-approval study was requested by FDA. This post-approval study will include a minimum of 45 subjects implanted by newly-trained surgeons at 5 to ten investigational sites followed through their 1-year follow-up visit for both safety and efficacy endpoints. In addition, an extension of the PMA pivotal clinical trial conducted under IDE G070162 was conducted as a separate post-approval study. That study demonstrated long-term safety and effectiveness through 5-year follow-up.

1.5 Duration of the Investigation

The post-approval study will commence immediately upon PAS Protocol approval. Subjects will be followed at 1, 4 and 10-months post-activation and annually thereafter through 1 year.

2 STUDY DESIGN AND OVERVIEW

2.1 Trial Design

This Post Approval Study is designed as a prospective, multi-center, non-randomized, clinical trial to evaluate the safety and efficacy of the *Esteem*® *System* implanted by newly-trained surgeons. For this trial the subject will act as his or her own control.

This trial has been designed to meet United States' regulatory requirements.

Each subject will act as both the test subject and the control by being tested prior to implant in both the unaided and aided condition.

2.2 Investigational Sites and Number of Enrollments

The post-approval study will enroll a minimum of 45 new subjects on a consecutive consenting basis at 5 to 10 investigational sites to be implanted by newly-trained surgeons. These subjects will be evaluated for both efficacy and safety endpoints. The goal will be to monitor the subjects through their one (1) year follow-up.
NOTE: In order to achieve the required sample size of 109 subjects for the safety endpoints, data from these 45 new subjects will be supplemented by data from a retrospective chart review of "commercial" (non-study subjects).

Trial Objectives

The overall objective of the study is to evaluate the safety and effectiveness of the *Esteem*® *System* implanted by newly-trained surgeons in subjects suffering from moderate to severe hearing loss.

Primary Objectives:

1) To demonstrate that the *Esteem® System* improves the speech threshold of sensitivity for hearing and identifying speech signals as well as or better than the pre-implant hearing aid (aided condition).

   Endpoint: Comparison of the speech reception threshold (SRT) using the *Esteem® System* as compared to the pre-implant aided condition.

2) To demonstrate that the *Esteem® System* is as effective as or better than the hearing aid for improving speech discrimination (intelligibility) as shown by the word recognition score at 50 dB.

   Endpoint: Comparison of word recognition score using the *Esteem®* as compared to the pre-implant aided condition.

3) To determine the incidence of Serious Adverse Device Effects (SADE) and Adverse Device Effects (ADE) and the incidence rate of device failures and replacements.

   Endpoint: The analysis of the incidence of SADEs and device failures and replacements at each follow-up.

4) To demonstrate that the incidence of facial pareses/paralysis is no greater than the 7% incidence experienced in the PMA clinical trial.

   Endpoint: The analysis of the incidence of facial pareses/paralysis at 1 month follow-up.

5) To demonstrate that the subjects' cochlear function remains unchanged with the *Esteem® System* as shown by comparison of the subjects' pre-implant baseline bone conduction threshold versus the subjects' post-activation visit bone conduction threshold.

   Endpoint: Comparison of the bone conduction threshold with forehead placement compared to the pre-implant bone conduction threshold.

Secondary Objectives:

1) To show that the *Esteem® System* improves Quality-of-Life when compared to the baseline aided condition as shown by APHAB scores.
2) To gather subject feedback and comments on the use of the *Esteem® System* relative to the pre-implant hearing aid (aided condition) as shown by the *Esteem®* Questionnaire.

3 BENEFITS/RISKS

Sponsor and the investigators have determined that the study is justified because the potential benefits outweigh the attendant risks. This has been confirmed by FDA in approving PMA P090018.

3.1 Potential Benefits

Hearing aids, cochlear implants, and semi-implantable hearing prostheses are some of the technologies available for the treatment of hearing loss. The *Esteem® System* has been developed as a fully implantable treatment option for adults who have hearing loss. The potential benefits that the *Esteem® System* may provide include:

- Better fidelity of sound
- Elimination of ear canal occlusion
- Elimination of maintenance issues associated with hearing aids, cochlear implants and semi-implantable hearing
- Improved cosmesis
- Improved ease of communication
- Improved audiometric thresholds
- Improved hearing in noise

devices

- Elimination of hearing aid type feedback
- Elimination of intolerable ear canal conditions such as eczema or infections caused by hearing aids
- Ability to hear continuously throughout the day (24/7).
- Improved hearing in reverberating rooms
- Longer battery life than hearing aids
- Reduction of the stigma of hearing impairment
- Improved quality of life
- Regain active lifestyle

3.2 Potential Risks

Subjects participating in this study are subject to some potential risks and complications associated with the implantation and use of the *Esteem® System*. The occurrence of adverse events may result in a revision surgical procedure, which may include device replacement or device removal.

The *Esteem®* implant procedure is a middle ear surgery, and the risk of a potential revision procedure after a middle ear surgery, including the implant of the *Esteem®* system may be as high as 7%. The revision rate for the subjects enrolled early in this clinical trial was 5% with an additional 2% explant rate.

The potential risks and discomforts associated with the operative procedure are similar to those for standard mastoid operations. Risks include but are not limited to the following:

- Bleeding
- Cerebral spinal fluid (fluid that surrounds the brain) leak and meningitis (brain infection)
- Damage to the Chorda Tympani branch of the facial nerve which may result in temporary or permanent taste disturbances
- Death
- Development of ear ringing (tinnitus) or an increase in ringing that was already present before the operation
- Drainage from ear canal
- Eardrum perforation/hole
- Hematoma/blood clot
- Infection of the ear
- Jaw soreness or stiffness
- Partial or complete one-sided facial paralysis or stimulation
- Partial or total loss of remaining hearing on implanted ear due to surgical procedure
- Physical breaking or dislocation of the middle ear bones
- Post-operative pain (everyone has discomfort after surgery for which we prescribe pain medication)
- Temporary external ear or incision numbness
- Transient or prolonged dizziness or vertigo
- Widening and thickening of the scar behind the ear (there is a small scar in every patient)
- Transient or prolonged ringing (tinnitus) in the operated ear

There may be some potential risks and complications that are possible due to the implantation and use of the *Esteem® System*. These risks include but are not limited to the following:

- Amplification of body sounds such as chewing or swallowing
- Cranial stimulation or head vibrations
- Decay of soft tissue or bone (includes erosion, necrosis, extrusion, or dehiscence of the wound) resulting in the body's rejection of the device
- Device failure/malfunction
- Loss of attachment of leads from the Sound Processor or the transducers from the mastoid and/or ossicular chain bones (incus or stapes) that requires surgery to fix
- Noise, distortion, or poor fidelity
- Non-implant of the device due to fit or function of the device

- Dizziness when test vibrations are delivered to the stapes (middle ear bone)
- Feedback/whistling or squealing from the device
- Fibrotic growth/keloid formation (growths around the scar tissues or around the device)
- Infection of the Sound Processor pocket
- Injury to the middle ear bones because of physical contact with the Sensor/Driver portion of the device
- Partial or total loss of remaining hearing on implanted ear due to device failure
- Stimulation of the chorda tympani branch of the facial nerve
- Stimulation of the facial nerve
- Subluxation of the stapes as a result of cement removal during revision or explantation of the *Esteem® System*
- Transient or permanent injury to the hearing (auditory) nerve of the test ear with subsequent hearing loss due to the physical vibration of the stapes by the Driver portion of the device
- Accumulation of air under the scalp around the Sound Processor due to inadvertent nose blowing after the operation

Potential risks to the ear include infection of the ear. Risks specific to the middle ear include but are not limited to the following:

- Fullness or stuffy sensation in the ear
- Middle ear infection
- Ossicular necrosis or deterioration of the middle ear bones over time
- Hearing loss secondary to other risks of the middle ear
- Reconstruction of the bony ossicular chain due to resection of the long process (arm) of the incus bone

Potential risks of cochlear damage include but are not limited to the following:

- Damage to the cochlea (inner ear) due to excessive pressure from the *Esteem System*
- Damage to the cochlea (inner ear) associated with performing intra-operative testing
- Excessive electrical stimulation from the device of the inner ear
- Excessive vibration of the inner ear
- Hearing loss secondary to other risks to the inner ear
- Insufficient stimulation of the inner ear

Potential risks associated with anesthesia include but are not limited to the following:

- Neurological complications due to an increase in general anesthesia time above that normally associated with mastoid surgery
- Reaction to anesthesia
- Allergic reactions

Potential risks associated with a second surgical procedure (a transcanal middle ear surgery) include but are not limited to the following:

- Disruption of the Sensor when lifting the eardrum
- Drainage from the ear canal
- Infection
- Injury to the nerve for taste (chordatympanineve) causing a temporary or permanent taste disturbance
- Pain from the surgical procedure
- Immediate or delayed hole(s) in the eardrum (perforation(s))
- Reaction to anesthesia
- Stiffening of the eardrum

All efforts will be made to minimize these risks by selecting investigators (includes surgeon, audiologist, technician, and/or research coordinator as appropriate for each site) who are experienced and skilled in otology. All investigators will be trained in the placement of the

Esteem® System prior to the start of the study. See Section 6.4 for Physician Training Plan.

These risks can be minimized through the use of strict aseptic technique, compliance with this protocol and technical implant procedures, adherence to the guidelines for subject selection, close monitoring of the subject's physiologic status during implant and follow-up procedures, and by promptly supplying Envoy Medical with all information required by this protocol.

4 TRIAL METHODOLOGY

4.1 Subject Selection

All subjects with moderate to severe sensorineural hearing loss are potential study candidates. The site is responsible for screening potential subjects and selecting those who are appropriate for *Esteem®* implant. Subjects who meet the inclusion / exclusion criteria will be asked to participate in the trial.

4.1.1 Inclusion Criteria

Subject must meet all of the following criteria to be eligible for treatment in the trial:

a) Subject is ≥ 18 years old

b) Subject understands the nature of the procedure and has signed the Subject Informed Consent Form prior to the procedure

c) Subject is willing and able to comply with specified follow-up evaluations and understands the audiological test procedures and use of the *Esteem® System*.

d) Subject has moderate to severe sensorineural hearing loss in the ear to be implanted defined by pure tone average air-conduction threshold level.

e) Subject has an unaided maximum word recognition score of greater than or equal to 40% with recorded delivery using a phonetically balanced word list at SRT + 40 dB or at maximum tolerable presentation level.

f) Subject is a current user of a properly functioning and appropriately fit hearing aid for at least one (1) month in the ear to be implanted.

g) Subject has normally functioning eustachian tube

h) Subject has normal tympanic membrane

i) Subject has a normal middle ear anatomy

j) Subject has adequate space for *Esteem® System* implant determined via fine cut temporal bone CT scan

k) Subject is a native speaker of the English language.

4.1.2 Exclusion Criteria

Subjects will be excluded from the trial if any one of the following criteria is met:

a. Subject has a history of post-adolescent chronic middle ear infections, inner ear disorders or recurring vertigo requiring treatment, disorders such as mastoiditis, Hydrops or Meniere's syndrome or disease

b. Subject has a history of otitis externa or eczema for the outer ear canal and the investigator believes this will affect the *Esteem® System* implantation
c. Subject has cholesteatoma or destructive middle ear disease
d. Subject has life expectancy of < two (2) years due to other medical conditions
e. Subject has retrocochlear or central auditory disorders
f. Subject is known to be suffering from any psychological, developmental, physical, or emotional disorder that the investigator feels would interfere with the surgery or follow-up testing
g. Subject has a known history of fluctuating air conduction and/or bone conduction hearing loss over a one-year period of 15 dB in either direction at 2 or more frequencies (from 500 – 4000 Hz)
h. Subject has sudden hearing loss due to unknown cause
i. Subject has a history of disabling tinnitus, defined as tinnitus which required treatment.
j. Subject is unable to adequately perform audiological testing
k. Subject has a medical condition or undergoing a treatment that may affect healing and the investigator does not believe the subject is a good candidate for the trial.
l. Subject has diabetes that is not well controlled with medication or diet and the investigator does not believe in his best medical judgment that the subject would be a good candidate for the trial
m. Subject is pregnant at the time of device implant
n. Subject has a history of keloid formation
o. Subject has known hypersensitivity to silicone rubber, polyurethane, stainless steel, titanium and/or gold

4.2 Screening and Baseline

Screening and baseline consists of a thorough evaluation of the subject's unaided and aided hearing to verify that the subject meets the entrance criteria and to serve as a baseline. The testing to be performed for the screening and baseline can be found in Table 1. All screening and baseline testing must be completed within 2 months of the *Esteem® System* implant procedure.

The screening process will begin with a review of the Screening and Baseline Subject Informed Consent Form. If the subject signs the Screening and Baseline Subject Informed Consent Form the subject will not be excluded from screening testing.

The screening will continue with an Audiological Pre-Screen. If the subject's audiological criteria do not exclude him or her from the trial, the subject's medical records will be reviewed to determine if the subject meets the basic screening criteria. If the subject's medical history does not exclude him or her from the trial, the *Esteem® System* clinical trial will be discussed with the subject and the subject will be asked to sign the Surgical Subject Informed Consent Form.

The screening will continue with basic audiological testing and high resolution CT scan to further evaluate the subject's eligibility for enrollment into the trial. If the subject has had a standard of care CT scan that shows adequate space for the *Esteem®* System implant, within 6 months of study screening procedures, this data will be acceptable for use in fulfilling the related inclusion criterion. This testing will consist of audiological testing in the unaided and aided condition.

In order to be implanted with the device, the subject must have worn an appropriately fit hearing aid for a minimum of 30 days prior to the *Esteem® System* implant procedure. An optimized fit for the pre-implant hearing aid will achieve insertion gain within +/- 10 dB of the gain recommended by the hearing aid manufacturer. Real Ear Measurement (REM) will be used to validate that the subject's hearing aid is properly fit to within ±10 dB (500 Hz

to 4000 Hz) of this optimized gain. If the subject meets all of the initial screening criteria, but does not have an appropriately fit hearing aid, the patient's hearing aid will be fit with the manufacturer's proprietary fitting program for the optimized fit for the patient. The REM data will be recorded on the Screening Case Report Form to validate optimal fit of the baseline hearing aid.

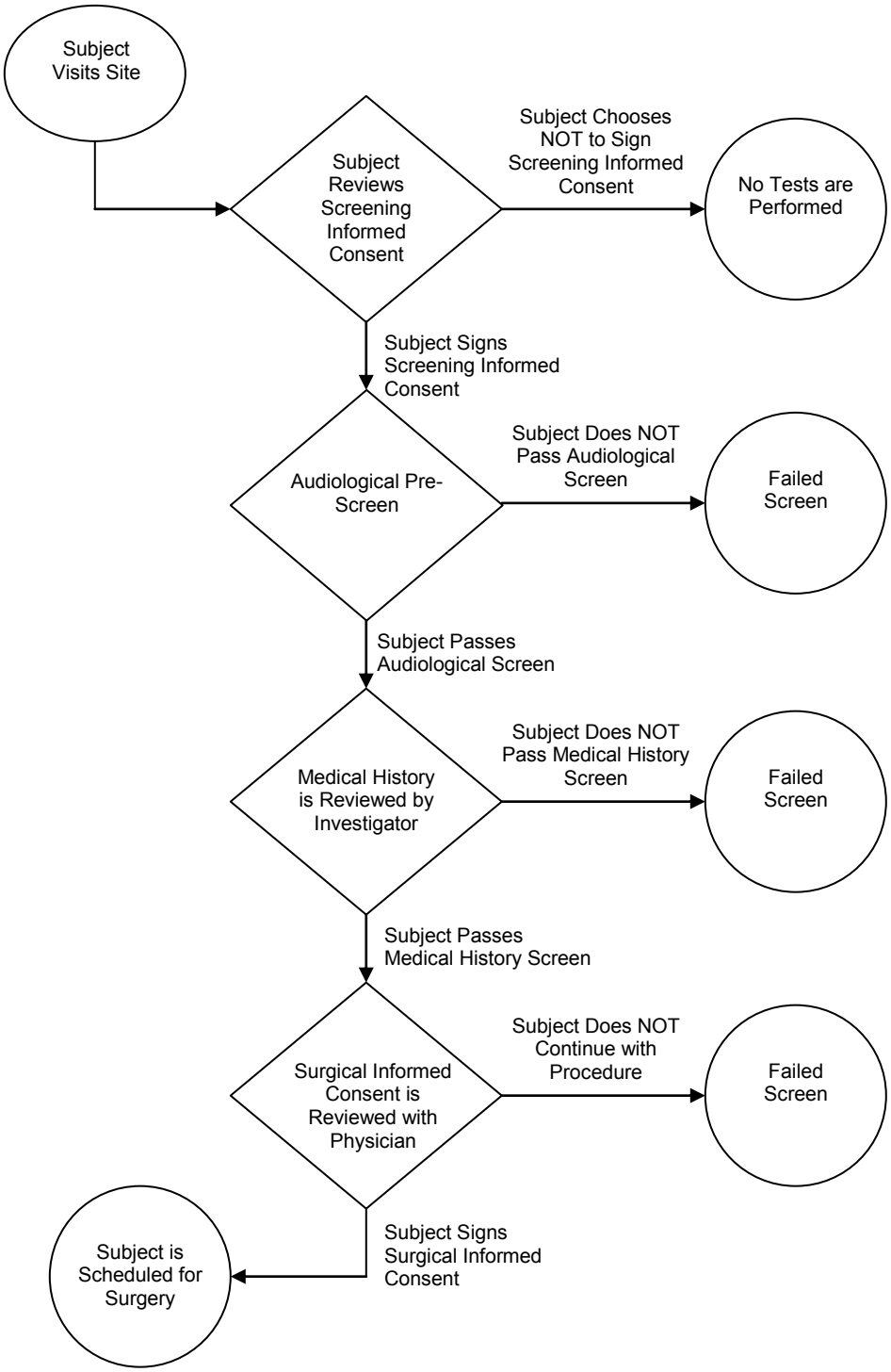
If the subject requires a new hearing aid or the subject's own hearing aid settings were adjusted, the subject will need to return a minimum of 30 days later to ensure that the subject is well adjusted to the new hearing aid. When the subject returns, all screening and baseline testing will need to be tested / re-tested. If the subject's hearing aid is appropriately fit but does NOT pass the REM enrollment criteria, and the subject declines to return 30 days later to repeat all screening and baseline testing as required for the REM criteria, the subject may still be enrolled but their audiometric data will not be included in the analysis of study efficacy endpoints (safety and adverse event data at least through 1-month follow-up will still be included).

If the subject's hearing aid did not require adjustment, the subject can proceed with the remainder of the screening and baseline procedures.

Following the screening and baseline testing, if the subject meets all of the Inclusion/Exclusion Criteria, the subject will proceed with the *Esteem® System* Implant.

This study is a non-randomized clinical trial. If the pure tone average (average of 500, 1K and 2K) for both ears is within 5 dB, it will be up to the Investigator and the subject to select the ear that is to be implanted.

Esteem® Post Approval Study Pre-Screen Process



4.3 Surgical Procedure

The surgical procedure for the implantation of the *Esteem® System* is outlined below. Subjects will be considered enrolled in the trial once they have signed the Informed Consent Form.

4.3.1 Preparation of the subject and *Esteem® System* placement

a) The subject will be anesthetized.

b) Prepare subject for intra-operative testing

c) Ensure that a facial nerve monitor is positioned to monitor the facial nerve during the procedure (use of this at surgeon discretion).

d) The replica Sound Processor may be used for determination of initial incision placement.

e) The incision will be made and the ear retracted for the creation of the mastoid cavity.

f) Use the replica Sound Processor to create a bed in the largest flat area of the temporal bone. The bed should be positioned so that the Sound Processor will lie as flat as possible without rocking. Note: The Sound Processor bed should be drilled first to prevent excess bone dust from getting into the facial recess. In addition, when drilling the SP bed care should be taken to prevent any penetration of the dura. A thin layer of bone should remain in the bottom of the SP bed for the SP to rest on. If the SP bed is drilled after the facial recess has been opened the facial recess and mastoid cavity should be packed to prevent bone dust from accumulating in the middle ear.

g) Create a channel for placement of the Driver/Sensor leads.

h) The facial recess will be opened to allow placement of the Driver.

i) Throughout the procedure the surgical site should be continuously irrigated with antibiotic solution.

j) Upon completion of the mastoidectomy and prior to separation of the ossicular chain, perform baseline test for comparison to *Esteem® System* implanted components and record results.

k) Separate the incus from the stapes and resect approximately 1mm to 3mm from the long process of the incus.

4.3.2 Driver and Sensor Placement

The placement order of the Sensor/Driver is at the discretion of the surgeon. The order of placement will be recorded on the *Esteem® System* Implant Worksheet.

a) After removing the Driver from the packaging, measure the capacitance using a capacitance meter. Compare the measured capacitance of the Driver to the capacitance value printed on the label of the shipping container. If the value is not within +/- 10% of the labeled value do not use the Driver. Record the labeled and pre-implant measured capacitance values.

b) Apply the first coating of EnvoyCem™ cement to the capitulum of the stapes, taking care to assure complete coverage.

c) Attach the Glasscock Stabilizer to the cortex of the temporal bone with bone screws in the base.

d) Insert the Glasscock Stabilizer in the stabilizer socket of the Driver.

e) Position the Driver transducer tip above the stapes and secure the Driver housing and legs to the mastoid floor using MedCem™ cement. After the Driver housing cement on the mastoid floor has set, connect the Driver transducer tip to the stapes using EnvoyCem™ cement.

f) Open and remove the Sensor from the packaging, measure the capacitance. Compare the measured capacitance of the Sensor to the capacitance value printed on the label of the shipping container. If the value is not within +/- 10% of the labeled value do not use the Sensor. Record the labeled and pre-implant measured capacitance values.

Note: One Glasscock Stabilizer may be used to position both the Sensor and Driver. If reusing the stabilizer and it has not been removed from the cortex skip to step h.

g) Attach the Glasscock Stabilizer to the cortex of the temporal bone with bone screws in the base.

h) Insert the Glasscock Stabilizer in the stabilizer socket of the Sensor.

i) Position the Sensor transducer tip in the suggested incus / malleus position and secure the Sensor housing and legs to the mastoid floor using MedCem™ cement.

j) After the Sensor housing bone cement on the mastoid floor has set, connect the Sensor transducer tip to the malleus and/or incus using EnvoyCem™ cement.

k) After all bone cement has set remove the Glasscock Stabilizers and bone screws from both the Sensor and Driver.

4.3.3 Intra-operative Testing

Once the Sensor and Driver have been positioned, testing will be performed using the Intra-operative System Analyzer (ISA). This testing may be performed in any order at the discretion of the surgeon.

NOTE: During the performance of the intra-operative testing the surgical site must be kept dry. Therefore, it may be necessary to drain fluid from the surgical site during the testing procedure.

4.3.3.1 Intra-operative Driver Testing

a) Connect the Driver to the driver cable.

b) Check the capacitance of the Driver and compare to pre-positioning value. If the value is not within +/- 10% of the labeled value remove the Driver and do not use. Record the post-implant capacitance on the CRF.

c) Conduct Laser Doppler Vibrometry (LDV) test to measure stapes displacement.

d) Compare the Driver signal strength at 1Vrms to the acceptance range according to the ISA.

e) Record the capacitance, and intra-operative test results.

4.3.3.2 Intra-operative Sensor Testing

a) Connect the Sensor to the sensor cable.

b) Check the capacitance of the Sensor and compare to pre-positioning value. If the value is not within +/- 10% of the labeled value remove the Sensor and do not use. Record the post-implant capacitance on the CRF.

c) Conduct the Sensor test.

d) Measure the Sensor signal strength in volts peak-to-peak.

e) Compare the Sensor signal strength at 100 dB to the acceptance range according to the ISA.

f) Record the Sensor signal strength and capacitance.

4.3.3.3 Intra-operative System Testing

The complete *Esteem® System* will be tested.

a) Interrogate the Sound Processor prior to opening the non-sterile shelf carton. If the Sound Processor does not respond to interrogation, do not use and return to Envoy Medical.

The following testing will be performed after the leads have been connected to the Sound Processor and prior to wound closure. The surgical site must be keep free of all fluids and as dry as possible during the system test to reliably collect valid test data.

b) Connect the Sensor and Driver connectors to the Sound Processor. Verify that the lead terminal pins are completely inserted into the SP lead barrels (the pin will be visible past the connector block).

c) Program the Sound Processor to perform the system test.

d) Perform the system test at 80 dB according to the ISA.

e) Record the system test results.

f) After completion of all testing, program the Sound Processor volume step to “OFF”

4.3.4 Placement of Sound Processor

Prior to the Sound Processor being placed in the Sound Processor bed the wound will be irrigated with an antibiotic solution. In addition if the subject is diabetic and the surgeon, using his best medical judgment, feels that the subject would benefit from an additional treatment the wound may be flushed with a 10% Fluconazole anti-fungal solution. After the Sensor and Driver connectors are inserted into the Sound Processor, the surgeon has the option to secure the Sound Processor with sutures, titanium straps or Gortex strips in the previously created bed. Verify that the Sound Processor fits tight and does not move. Position the Driver/Sensor leads in the previously created channels and secure to prevent the leads from crossing, touching, or rubbing. After all testing is complete the surgeon will close the incision.

4.4 Post-Procedure/Discharge

Prior to discharge, the investigator may take an x-ray of the implanted device to visualize the location of the device so that leads are not accidentally cut in the event of a battery exchange or a system revision is required. The Investigator will also assess the subject’s clinical status and record any clinical events. It is recommended that any subject that is diabetic would be administered an oral prophylactic antifungal treatment of either

Fluconazole or Voriconazole for two weeks post-operatively. This treatment should be given only if in the investigator's best medical judgment and after a careful review of the subject's medical status and history.

The Investigator/Audiologist/Research Coordinator will review the follow-up requirements with the subject to ensure compliance with the follow-up schedule. Subjects will be reminded of the requirements for follow-up.

4.5 Follow-Up

Post-implant, the subjects will be required to return for follow-up and testing of the *Esteem® System* as listed below.

All subjects will return to the investigator/audiologist for the scheduled clinical and audiological follow-up visits. Follow-up testing should be performed in the same clinic/laboratory as the baseline testing whenever possible. The testing for each visit is outlined in Table 1.

Due to the complexity of the device, Envoy Medical personnel may be present at the follow-up visits in order to assist the site personnel on programming methods.

4.5.1 Post Implant Follow-up Visit(s)

The investigator may schedule as many post surgical visits as he/she feels are necessary to evaluate each subject's healing status. The investigator should ensure proper healing of the middle ear and around the SP. These visits may be scheduled as needed until the Activation Visit, at which time the protocol defined time frames must be followed.

4.5.2 Activation Visit (8 weeks ± 2 week post implant)

At the Activation visit, the subject will be evaluated to ensure proper healing of the middle ear and around the implanted Sound Processor. The device will be turned on to begin the acclimation period. An audiogram will be performed along with an *Envoygram* to ensure that the device is providing the subject with some benefit.

The testing required at the Activation Visit is outlined in Table 1.

A personal programmer will be provided to the subject and he or she will be instructed on how to use the Personal Programmer prior to leaving the clinic.

Due to the nature of Middle Ear surgery and potential requirements for multiple revisions, the surgical procedure may require a second procedure or "revision" to properly adhere the driver to the stapes. The procedure will be considered complete once the driver to the stapes connection has been determined to be successful by the surgeon. All revision surgeries will be reported as clinical procedure failures.

4.5.3 Follow-up Visits

The subjects will return to the clinic for follow-up visits after the device is activated. The visits will occur at 1 month (± 3 weeks), 4 months (± 3 weeks) and 10 months (±3 weeks) post activation. The visits will consist of the testing outlined in Table 1.

4.6 Testing Requirements

Testing requirements for the trial are listed in table 1.

TABLE 1: Minimum Screening and Follow-up Requirements

	Scr / BL	Proc/ Disc	Act	1 Mo	4 Mo	10 Mo
Informed Consent	X					
Medical History	X					
Audiological and Hearing Aid History	X					
Current Medications	X		X	X	X	X
Adverse Events			X	X	X	X
Device Settings			X	X	X	X
Testing Requirements						
APHAB Questionnaire	X				X	X
Esteem® Questionnaire					X	X
Otoscope Exam (perform prior to testing)	I/N		I	I	I	I
Tympanogram	I/N		I	I	I	I
Air Conduction Thresholds	I/N		I	I	I/N	I/N
Air Conduction – Aided (Implant) Ear Warble Tone	I			I	I	I
Bone Conduction Thresholds	I/N		I	I	I/N	I/N
Most Comfortable Listening Level (MCL)	I/N		I	I	I	I
Uncomfortable Listening Level (UCL)	I/N		I	I	I	I
Speech Reception Threshold (SRT)– unaided	I/N					
Speech Reception Threshold (SRT)– aided	I/N		I	I	I	I
Word Recognition – unaided	I/N					
Word Recognition – aided	I/N		I	I	I	I
Envoygram IT			X	X	X	X
CT Scan	X					
X-ray of implanted device (optional)		X				

I=Implanted Ear N=Non-Implant Ear

4.6.1 Device Revisions / Interventions

There is also a possibility that post-implant, a surgical intervention may be required to repair, replace or completely remove some or all of the components of the *Esteem® System* due to device failure, malfunction or as a result of an adverse event. The surgical procedure may be performed in one of two ways: either through the subject's original incision or through the external ear canal; depending on the scope of the intervention. The surgical procedure may be performed under local or general anesthesia at the discretion of the surgeon.

A description of the recommended procedure that will be followed for each revision method is listed below:

4.6.1.1 Mastoid Approach (through the original incision)

- The original incision will be opened to expose the Sound Processor (SP).
- The Driver and Sensor lead will be disconnected from the SP.
- The capacitance of the Driver and Sensor will be tested.
- The Driver and Sensor will be tested. All or some of the intra-operative testing may be preformed in order to evaluate the system.
- The test results will be evaluated to determine if the Driver and Sensor are functioning correctly. If one or both are not performing as expected the non-functioning part will be removed and replaced with a new part following the standard implant techniques outlined above. The new part will be tested to verify correct function.
- The Driver and Sensor will be connected to the Sound Processor, system testing will be performed and the wound closed.

4.6.1.2 Ear Canal Revision

This approach will only be used to give access to the Driver/stapes interface. No part of the device will be removed or replaced using this approach. It is possible that the bone cement may be removed and reapplied.

- An incision will be made in the ear canal close to the tympanic membrane (TM).
- The TM will be lifted away to expose the Driver/stapes interface for evaluation.
- If the bone cement requires replacement the old cement will be removed and new cement will be placed.
- Laser Doppler Vibrometer (LDV) measurements may be made.
- The TM will be replaced and the outer ear canal will be packed.

All revisions will be documented in the subject CRFs.

4.6.2 Removal of Subjects from Study

All subjects enrolled in this study are subject to complete clinical follow-up and will be included in the analysis of safety and effectiveness, as appropriate.

A subject may be removed from the study for any of the following reasons:

- Subject has fulfilled Protocol Requirements
- Subject did not receive the implant
- Subject withdraws consent
- Subject is lost to follow-up

- Subject has an inter-current illness that precludes follow-up
- Subject does not comply with the protocol
- Subject dies
- Investigator believes that it is in the best interest of the subject
- Sponsor terminates the study

If the subject completes or is withdrawn from the study the reason will be recorded on the CRF along with any relevant information concerning any device explant, subject death, and autopsy.

4.7 Adverse Events

The 109 subjects to be reported for the Adverse Event endpoint will consist of the 45 newly-implanted subjects supplemented by data from a retrospective chart review of “commercial” (non-study subjects).

4.7.1 Definitions

Adverse Event (AE): An Adverse Event is any undesirable clinical event occurring to a subject, during a clinical trial, whether or not it is considered related to the investigational product. This includes a change in a subject's condition or laboratory results, which has or could have a deleterious effect on the subject’s health or well-being, including failure of bone conduction/safety algorithm.

Serious Adverse Event (SAE): A Serious Adverse Event (SAE) or a Serious Adverse Device Effect (SADE) are events which:

- Results in death
- Is life threatening
- Results in persistent or significant disability / incapacity
- Results in a congenital anomaly / birth defect
- Requires or prolongs in-patient hospitalization (>24 hours)
- Requires intervention to prevent permanent impairment/damage

Unanticipated Adverse Device Effect (UADE): An Unanticipated Adverse Device Effect is any serious adverse effect on health or 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 (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. NOTE: an UADE is, by definition, serious in nature.

4.7.2 Reporting of Adverse Events

The procedure for reporting any AE is as follows:

- All Adverse events will be documented on an Adverse Event Form
- The Investigator is responsible for reporting AEs to his or her IRB in accordance to their site's IRB procedures.
- The Investigator shall report all unanticipated adverse device effect to the Monitor/Sponsor as soon as possible, but definitely no later than 10 days after obtaining knowledge of event.
- The Sponsor is responsible for informing the FDA, all reviewing IRBs and other investigators of any unanticipated adverse device effect that has occurred.

4.8 Device Failures and Malfunctions

4.8.1 Definition: A Device failure is defined as the inability of the device to perform its intended function. Device failures can result from hardware/software problems or surgical procedure problems.

4.8.2 Reporting and Return: All failures and malfunctions will be documented on the CRF and reported in the clinical results. *Esteem® System* devices that fail or malfunction will be returned to the Sponsor for analysis.

If at all possible, a representative from the Sponsor will be present for the removal of an *Esteem® System* due to a failure or malfunction.

5 STATISTICAL ANALYSIS

5.1 Sample Size

For the effectiveness objectives, based upon the following analysis and 0204 clinical data, a sample size of 45 new subjects meets the guidelines for statistical power. For the facial pareses/paralysis objective with an end point of 1 month, a sample size of 109 subjects is required as shown below.

SRT
Based on a mean improvement in SRT over hearing aid of 10 dB and a standard deviation of 13 dB, 45 subjects at 1 year would provide at least 80% power for testing non-inferiority and superiority at a one-sided 0.05 alpha level. A margin of – 5 dB will be used for non-inferiority and a margin of +5 dB will be used for superiority.

WRS
Based on a mean improvement in WRS over hearing aid of 22% and a standard deviation of 31, 45 subjects at 1 year would provide at least 80% power for testing non-inferiority and superiority at a one-sided 0.05 alpha level. A margin of –10% will be used for non-inferiority and a margin of +10% will be used for superiority.

Facial Pareses/paralysis:
Based upon a null hypothesis of 7% and a hypothesized true rate of 2% of facial paresis/paralysis, 109 subjects at 1 month would provide at least 80% power for testing the hypothesis.

5.2 Objective Analysis

The following statistical analyses will be done.

Objective 1: To determine whether the *Esteem® System* improves the subjects' threshold of sensitivity for hearing and identifying speech signals as well as or better than the pre-implant conventional hearing aid.

Endpoint: Comparison of the subjects' speech reception threshold using the subjects' pre-implant aided condition as compared to the *Esteem®* at follow-ups of 4 months to 1 year.

Criterion for Non-Inferiority- The 95% Lower Confidence Bound (LBC) for the mean difference between the SRT at baseline versus follow-up ($\mu_{\text{Pre-implant aided} - \text{follow-up}}$) is greater than or equal to -5 dB.

$$\text{95\% LCB for } \mu_{\text{Pre-implant aided} - \text{follow-up}} \geq -5$$

Criterion for Superiority- The 95% Lower Confidence Bound (LCB) for the mean difference between the SRT at baseline versus follow-up ($\mu_{\text{Pre-implant aided} - \text{follow-up}}$) is greater than +5 dB.

$$\text{95\% LCB for } \mu_{\text{Pre-implant aided} - \text{follow-up}} > +5$$

Category Analysis: In addition, the results will be categorized by level of improvement, showing % of subjects at each improvement/unimprovement category compared to pre-implant aided condition with the categories of improved/unimproved based on the +/- 5 dB margins.

Objective 2: To demonstrate that the *Esteem® System* is as effective as or better than the hearing aid for improving speech discrimination (intelligibility) as shown by the word recognition score at 50 dB.

Endpoint: Comparison of the word recognition score using the *Esteem®* compared to the pre-implant aided condition at follow-up from 4 months to 1 year.

Criterion for Non-Inferiority- The 95% Lower Confidence Bound (LBC) for the mean difference between the WRS at baseline versus follow-up ($\mu_{\text{Pre-implant aided} - \text{follow-up}}$) is greater than or equal to -10%.

$$\text{95\% LCB for } \mu_{\text{Pre-implant aided} - \text{follow-up}} \geq -10\%$$

Criterion for Superiority- The 95% Lower Confidence Bound (LCB) for the mean difference between the WRS at baseline versus follow-up ($\mu_{\text{Pre-implant aided} - \text{follow-up}}$) is greater than +10%.

$$\text{95\% LCB for } \mu_{\text{Pre-implant aided} - \text{follow-up}} > +10\%$$

Additional Analyses: The Word Recognition Scores will be compared using the Thornton and Raffin (1978) published upper and lower limits for various word lists based upon percentage scores. Based upon this, an analysis of the % better than, % equal to and % below the aided condition (HA) will be presented.

Reference:
Thornton AR, Raffin MJ. Speech discrimination scores modeled as a binomial variable. J Speech Hear Res 1978; 21:507-18.

Objective 3: To determine the incidence rate of Serious Adverse Device Effects (SADE) and the incidence rate of device failures and replacements.

Endpoint: The analysis of the incidence of SADEs and device failures and replacements at each follow-up.

Hypotheses: There is no formal hypothesis. This objective is to provide an accurate estimate of the SADE rate and device failure and replacement rate associated with the *Esteem® System*.

Statistical Analyses: The incidence of SADEs and device failures and replacements will be estimated with the observed number of SADEs and device failures and replacements over the total person-months of follow-up at each follow-up. The upper bound of the one-sided 95% exact binomial confidence interval on the SADE rate and device failure and replacement rate will be calculated and reported.

Objective 4: To demonstrate that the incidence of facial pareses/paralysis is no greater than the 7% incidence experienced in the PMA clinical trial.

Endpoint: The analysis of the incidence of facial pareses/paralysis at 1 month follow-up.

Criterion for success: The 95% Upper Confidence Bound (UCB) for the incidence of facial paresis/paralysis ($p_{\text{paresis/paralysis}}$) is less than 7%

$$\text{95\% UCB for } p_{\text{paresis/paralysis}} < 7\%$$

Statistical Analyses: The upper bound of the one-sided 95% exact binomial confidence interval on the incidence of facial paresis/paralysis will be compared to 7% and success declared if it is lower than 7%.

Objective 5: To demonstrate that the subject's cochlear function remains unchanged with the *Esteem®* system as shown by comparison of the subject's pre-implant baseline Bone Conduction Threshold (BCT) vs. the subject's post activation BCT.

Endpoint Analysis: Bone conduction will be measured with forehead probe placement. The Safety Algorithm as described in Attachment C, will be used for any Bone Conduction results outside the stability range.

6 ADMINISTRATIVE RESPONSIBILITIES

6.1 Institutional Review Board (IRB)

This protocol and the informed consent must be reviewed and approved by each site's IRB prior to obtaining written informed consent or allowing a subject to participate. Changes to the protocol that may increase the risk or present new risks to the subject, or may adversely affect the validity of the trial, must be approved in writing by Sponsor, IRB and the FDA before the change is made.

IRB approval to participate in this trial is required from each institution participating in this investigation. Prior to subject enrollment, a signed copy of the IRB approval letter must be submitted to Sponsor certifying trial approval. Investigators are responsible for submitting and obtaining initial and continuing review (at intervals not greater than once a year) of the trial by their IRB.

The investigator will report to the Sponsor immediately, if, for any reason, the approval to conduct the investigation is withdrawn. The report will include a complete description of the reason(s) for which the approval was withdrawn.

6.2 Subject Informed Consent

Prior to screening for eligibility, subjects must consent to screening and baseline testing. During the consent process, the scope, and the description of tests of the screening and baseline should be reviewed with the subject. The subject should have the option to ask questions and have them answered to their satisfaction. The process of consenting the subjects must be documented on the screening and baseline informed consent form.

Prior to enrollment into the trial, subjects must consent to participate in the trial. During the consent process, the scope, requirements, risks and benefits of the trial should be reviewed with the subject. The subject should have the option to ask questions and have them answered to their satisfaction. The process of consenting the subjects must be documented on the Surgical Informed Consent Form.

The template Surgical Subject Informed Consent Form and Screening & Baseline Informed Consent Form for this trial is located in Attachment A. Any adaptation of this format must include the elements of Informed Consent as required by 21CFR Part 50. The Informed Consent used must be approved by the Sponsor and the Institutional Review Board (IRB) prior to its use.

A copy of the signed IRB approved Surgical Subject Informed Consent Form and Screening and Baseline Subject Informed Consent Form must be retained at the investigational site along with the other investigational forms. A copy of the consent form is to be given to the subject.

6.3 Confidentiality

All information and data sent to Sponsor concerning subjects or their participation in this trial will be considered confidential by the Sponsor. Only authorized Envoy Medical personnel and their designees (including contract research organizations), advisory committees, Investigators at other sites and IRBs will have access to these confidential files and have the right to inspect and copy all of the records pertinent to this trial. This may include medical information gathered prior to the onset of this trial. Authorized FDA personnel also have the right to inspect and copy all records pertinent to this trial. All data used in the analysis and reporting of this evaluation will be without identifiable reference to the subject.

Data collected and stored at the Sponsor will be free of identifying information of the subject including subject names and medical records numbers.

In order to comply with the Health Insurance Portability and Accountability Act (HIPAA) that became effective April 14, 2003 in the US all subjects enrolled in the trial will be required to provide authorization to disclose Protected Health Information (PHI).

6.4 Investigator Training

All investigators chosen to participate in the *Esteem® System* Post Approval Study are qualified by training and experience in otolaryngology therapy and surgery and have special expertise in the field of clinical research relating to the trial.

Sponsor will schedule training on the surgical procedure for each of the participating investigators.

Training will consist of a discussion of the scientific basis for the *Esteem® System*, indications for the device, pre-operative assessment of temporal bone CT scan, the sequence and positioning of the Driver and the Sensor. The training will include a discussion on the programmable features of the Sound Processor. Work in the temporal bone lab for hands on experience with the mastoidectomy; positioning the Sensor and Driver; and implantation of the *Envoy* Sound Processor will be included as part of training. Each participant will implant approximately 2 *Esteem® Systems* in temporal bones during training.

In addition, all site personnel will be trained on the clinical trial protocol, the CRF completion procedures, the regulations pertaining to conducting clinical trials, study processes, device handling, and the *Esteem® System* programmer.

The audiologists at each site will be trained on the use of the *Esteem*® Programmer. This training will include a discussion on the programmable features of the Sound Processor.

In addition, a representative from Envoy Medical will be present at all of the implant procedures to perform intra-operative testing and advise the investigators if needed, and at the initial clinical follow-ups to answer any questions and help set up the device program with the site audiologist.

All training will be documented in the clinical site files at the sponsor.

6.5 Investigators Responsibilities

In accordance with FDA regulation 21 CFR Part 812 the investigator is responsible for ensuring that the investigation is conducted according to this protocol and that signed informed consent is obtained from the subject prior to his inclusion in the study. It is the investigator's responsibility to ensure that all staff assisting with the trial have appropriate qualifications, are fully instructed on the trial procedures and will respect confidentiality.

6.6 Data Monitoring and Quality Control

6.6.1 Training

The training of appropriate clinical site personnel will be the responsibility of Sponsor. To ensure uniform data collection and protocol compliance, personnel from Sponsor will review the Investigational Plan, techniques for the identification of eligible subjects, instructions on data collection, methods for soliciting data from alternative sources, and schedules for follow-up with the research coordinator and audiologist.

6.6.2 Case Report Forms (CRFs)

CRFs will be used to collect all subject data during the trial. CRFs will be monitored following the guidelines established by Sponsor's Standard Operating Procedures (SOPs).

6.6.3 Data Reporting

All data should be recorded on the site's standard source documentation.

The investigator, or an individual designated by him/her, is responsible for transferring the information to the appropriate CRFs. The data on each CRF must be legibly handwritten with a blue/black ballpoint pen. The investigator is responsible for the quality of the data collected and recorded during the trial.

The investigator is required to sign the CRF on the appropriate page(s) to verify that he/she has reviewed the recorded data..

6.6.4 Data Review

All CRFs will be reviewed for completeness and clarity upon receipt by Sponsor. Missing or unclear data will be requested as necessary throughout the trial. Sponsor will request further documentation such as physician procedure notes when SAEs, and/or malfunctions are observed and reported.

Data entry and development of the primary database for the trial will be performed by Sponsor or their designee(s). Sponsor or designee(s) will also be responsible for auditing the database and confirming the overall integrity of the data.

Sponsor or designee will provide clinical monitoring, including review of CRFs and parity checks with the source documentation including operator worksheets retained with CRF documentation and hospital charts.

All clinical sites will be monitored routinely for timeliness of CRF submission to Sponsor. Any evident pattern of non-compliance with respect to the timeliness will initiate remedial actions. If corrective actions are not subsequently undertaken, the clinical site may be withdrawn.

To this end, the Principal Investigator must permit inspection of the trial files and subject CRFs by such representatives and/or responsible government agencies.

6.7 Record Maintenance

6.7.1 Records

Records to be maintained by the investigator in a designated clinical trial administrative file include:

- Clinical trial investigational plan and all amendments
- Signed clinical trial agreement
- IRB approval letter(s) including informed consent
- IRB membership list or compliance assurance statement
- Correspondence relating to the trial
- Curriculum Vitae (CVs) for all investigators (Principal and Co-investigator), audiologist and research coordinator
- Site personnel signature list
- Sponsor personnel sign-in log
- Blank sets of CRFs and instructions for completion
- Subject enrollment log
- Investigational device inventory log with invoices, including: date, quantity, serial numbers of all devices, and identification of all persons the device was used on (subject identification log)
- Log of all devices returned to the Sponsor and the reason for the return
- Device manual(s) and/or Instructions for Use (IFU)

7 REPORTS (INCLUDES ANNUAL REPORTS, FINAL REPORTS FROM INVESTIGATOR AND SPONSOR)

The following records must be maintained for each subject enrolled in the trial:

- Signed *Esteem® System* Subject Informed Consent Form
- All completed CRFs
- Record of and supporting documentation for any AEs.
- Procedure reports, nursing notes, and subject office files
- Records pertaining to subject death during the investigation (including death records, death certificate, and autopsy report, if performed)

Sponsor recommends that the investigator retain copies of procedure reports, procedure nursing notes, audiologist's reports and the results of any procedures that occur post trial procedure.

7.1.1 Reports

Investigators are required to prepare and submit to Sponsor complete, accurate and timely reports on this investigation when necessary.

Records and reports will remain on file for a minimum of two (2) years after the completion/termination of the investigational trial. They may be discarded upon notification by Sponsor. To avoid error, the principal investigator should contact Sponsor before the destruction of any records and reports pertaining to the trial to ensure they no longer need to be retained.

In addition, Sponsor should be contacted if the principal investigator plans to leave the investigational site so that arrangements can be made for transfer of records.

7.1.2 Investigator's Final Report

Upon completion or termination of the *Esteem® System* clinical trial, the principal investigator must submit a final written report to Sponsor and their IRB. The report must be submitted within three (3) months of completion or termination of the trial.

7.2 Investigational Site Monitoring Procedure

Envoy Medical will serve as the Sponsor of the *Esteem® System* clinical trial, and Envoy Medical or their designee will monitor the trial according to Envoy Medical's Standard Operating Procedures (SOPs) and specific FDA regulations.

7.3 Labeling: Instructions for Use

Copies of the proposed Instructions for Use for the *Esteem® System* are included as a separate document.

7.4 Deviations from Protocol

The investigator shall not deviate from the protocol without the prior written approval of Sponsor except in medical emergencies or in unforeseen, isolated instances where minor changes are made that will not increase the subject's risk or affect the validity of the trial. In medical emergencies, prior approval for protocol deviations will not be required, but Envoy Medical Personnel or their designee must be notified within five (5) working days of the incident. All protocol deviations must be documented as to the nature of the deviation and the reason for the deviation on the appropriate CRF.

7.5 Investigational Site Termination

Envoy Medical reserves the right to terminate an investigational site for any of the following reasons:

- Failure to secure subject informed consent
- Failure to report UADEs within 10 days of knowledge of the event
- Repeated protocol violations
- Repeated failure to complete case report forms
- Failure to enroll an adequate number of subjects
- Loss of or unaccounted for investigational product inventor

ATTACHMENT A: *Safety Algorithm*

Bone Conduction/Safety Algorithm

Introduction

Bone conduction (BC) using forehead probe placement will be the primary test for cochlear function stability. While forehead placement will minimize some of the test variability issues associated with the mastoid probe placement as detailed in IDE G000321, there remains the possibility that BC test-retest variability may result in test results outside the ±10 dB limits due to equipment limitations and probe placement. As an improvement over the methods used in IDE G000321, the Safety Algorithm has been refined for use in this new clinical trial. In addition to bone conduction, the EnvoyGram function will be used as an in-situ audiogram to directly stimulate the cochlea. This method will be more accurate and a better indicator of cochlear stability than the previous EnvoyGram tests where testing done at implant was used to predict future performance.

The EnvoyGram IT

In addition to the programmable parameters used to affect the incoming signal, the Sound Processor has an internal tone generator that can be accessed through the *Esteem*® Programmer in a test mode called the EnvoyGram IT (EnvoyGram In-situ).

Simply put, the EnvoyGram IT is an in-situ audiogram utilizing the Driver to test cochlear function. When entering this test mode, the Sensor is deactivated. The *Esteem*® Programmer software allows the audiologists to select a frequency in the range 250 to 4000 Hz and amplitude in the range 55 to 119 dB SPL. The Sound Processor synthesizes and delivers a pure tone signal to the Driver to induce known vibrations directly into the cochlea. There are twelve steps of amplitude. Each step provides a 4 - 6 dB increase over the previous step. The typical EnvoyGram IT levels are based on:

a. a typical intact chain displacement of 40 nm at 100 dB for frequencies below 1 kHz (Validated per ASTM F 2504 and EMC 003798-001),

b. a typical Model 7502 Driver displacement in temporal bones of 88 nm/V (Validated per EMC 003798-001), and

c. a typical SP tone output for each volume and tone setting (Validated per EMC 003788-101 and EMC 003872-001).

Each patient's intact chain has a unique displacement profile. During implant of the *Esteem*® , intact chain data is measured and recorded to provide a normalization factor for the EnvoyGram IT.

Intra-operative data, ASTM F 2504, and temporal bone studies at Envoy (i.e. EMC 003798-001) all indicate that patient-to-patient variability of intact chain displacement is at least ±6 dB. ASTM F 2504 cites a 95% confidence interval of ±6 dB in temporal bones. Clinical experience has also shown that accurately quantifying the intact chain displacement of each patient in a live surgical field is also limited to approximately ±6 dB, due to presence of fluid in the middle ear space, available LDV laser angle, etc.

The EnvoyGram IT test protocol is similar to that of an audiogram. The intact-chain measurements are recorded on the Procedure and Discharge CRF (EMC 003900-003) and entered into the EnvoyGram IT by the audiologist. The test methodology is performed consistent with the Hughson-Westlake procedure. A signal is presented at the prescribed amplitude and frequency. If the subject acknowledges the signal, the intensity level is decreased two steps (10 - 12 dB). If that signal is not acknowledged, the intensity level is increased one step (6 dB), thus determining a threshold. This threshold provides a measure of cochlear function independent of the external auditory mechanism.

EnvoyGram IT SPL levels are customized to the patient by taking into account each patient's IC data. For instance, a patient with typical 40 nm IC displacement at 100 dB will have levels from 55 to 117 dB, but a patient with stiff 20 nm IC displacement at 100 dB will have levels from 61 to 123 dB. The table below lists the EnvoyGram levels for a) a typical intact chain displacement of 40 nm at 1.0 kHz, 100 dB SPL, b) an intact chain displacement of 20 nm at 1.0 kHz, 100 dB SPL, and c) an intact chain displacement of 80 nm at 1.0 kHz, 100 dB SPL.

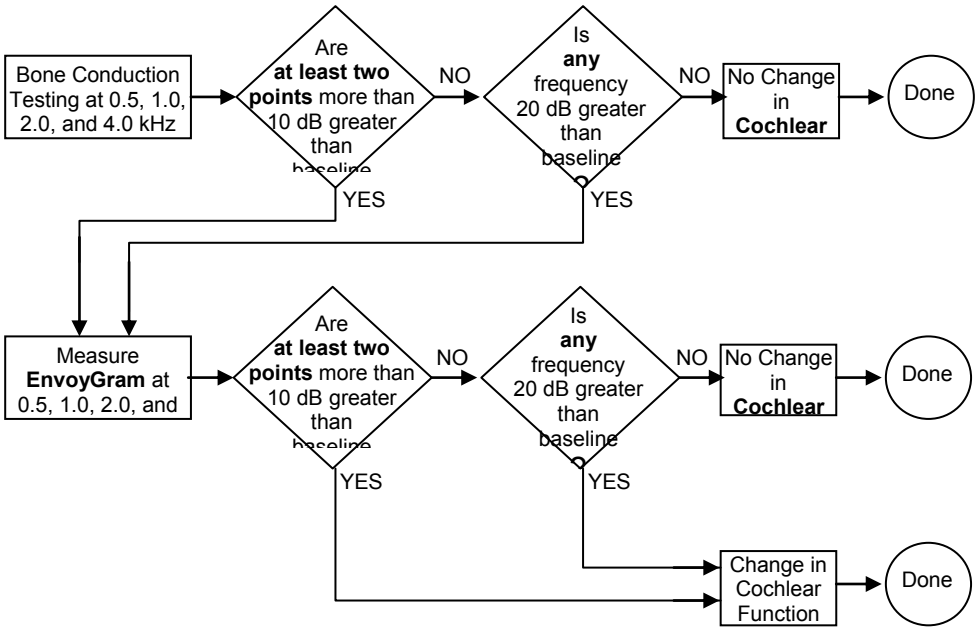
Table 1: EnvoyGram IT levels in *Esteem*® Programmer after intra-operative IC data entry. EnvoyGram IT levels are listed in dB SPL and are automatically calculated in

the *Esteem*® Programmer for each patient's IC data collected during implant procedure. These are the levels available for each of the test frequencies.

Typical (40nm IC @ 100dB SPL)	34	40	46	52	58	64	70	76	82	88	94	100
Stiff (20nm IC @ 100dB SPL)	40	46	52	58	64	70	76	82	88	94	100	106
Loose (80nm IC @ 100dB SPL)	28	34	40	46	52	58	64	70	76	82	88	94

Since the EnvoyGram IT levels are calibrated to each patient, the "predicted" EnvoyGram IT thresholds are equal to the baseline pre-implant unaided audiogram for each test frequency. For instance, a patient with 55 dB baseline air conduction threshold at 1 kHz and 80 nm measured IC would have a predicted EnvoyGram IT of 58 dB at 1 kHz (first level above baseline unaided threshold of 55 dB).

Bone Conduction/Safety Algorithm



Safety Algorithm Explanation:

The first level of the safety algorithm will use standard bone conduction (BC) thresholds. Bone conduction thresholds are measured in the implanted ear at 0.5, 1.0, 2.0, and 4.0 kHz at baseline and follow-up visits. If less than two (2) of the follow-up thresholds are more than 10 dB greater than the baseline thresholds, then the individual test frequencies are evaluated. At each test frequency, if the follow-up threshold is less than 20 dB greater than the baseline threshold then the algorithm is considered complete, with a conclusion that no change cochlear function occurred. However, if at least two (2) of the thresholds have increased more than 10 dB or if any individual threshold has increased by 20 dB or more, then the EnvoyGram data is evaluated.

The second level of the safety algorithm will use EnvoyGram thresholds. Baseline unaided air conduction pure tone thresholds at 0.5, 1.0, 2.0, and 4.0 kHz are measured at baseline. Similarly, EnvoyGram thresholds are measured in the implanted ear at 0.5, 1.0, 2.0, and 4.0 kHz at follow-up visits. Based on the intra-operative intact chain data, an EnvoyGram equivalent dB threshold is calculated for each of the four test frequencies. If less than two (2) of the follow-up EnvoyGram thresholds are more than 10 dB greater than the baseline thresholds, then the individual test frequencies are evaluated. At each test frequency, if the follow-up EnvoyGram threshold is less than 20 dB greater than the baseline threshold

then the algorithm is considered complete, with a conclusion that no change in cochlear function occurred. However, if at least two (2) of the EnvoyGram thresholds have increased more than 10 dB or if any individual EnvoyGram threshold has increased by 20 dB or more, then the algorithm is considered complete with a conclusion that a change in cochlear function occurred.

For patients with moderate to severe sensorineural hearing loss, non-responses (NR) are not uncommon during bone-conduction testing. If an NR occurs during baseline bone conduction testing, that test frequency is not evaluated (for the same patient) in the follow-up bone conduction portion of the safety algorithm. However, if an NR occurs during follow-up bone conduction testing (and is not preceded by a baseline NR at the same test frequency), the corresponding EnvoyGram threshold is substituted at the bone conduction NR test frequency.