DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 20, 2014

Mr. Sean Bundy
Cochlear Americas
13059 East Peakview Avenue
Centennial, CO 80111

Re: P130016
Nucleus® Hybrid™ L24 Cochlear Implant System
Filed: June 3, 2013
Amended: June 13, August 16, August 19, September 16 and December 09, 2013;
Procode: PGQ

Dear Mr. Bundy:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Nucleus® Hybrid™ L24 Cochlear Implant System. The Nucleus® Hybrid™ L24 Cochlear Implant System is intended to provide electric stimulation to the mid-to-high frequency region of the cochlea and acoustic amplification to the low frequency regions, for patients with residual low frequency hearing sensitivity.

The system is indicated for unilateral use in patients aged 18 years and older who have residual low-frequency hearing sensitivity and severe to profound high frequency sensorineural hearing loss, and who obtain limited benefit from appropriately fit bilateral hearing aids. Typical preoperative hearing of candidates ranges from normal to moderate hearing loss in the low frequencies (thresholds no poorer than 60 dB HL up to and including 500 Hz), with severe to profound mid to high frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥75 dB HL) in the ear to be implanted, and moderately severe to profound mid to high frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥ 60 dB HL) in the contralateral ear. The CNC word recognition score will be between 10% and 60%, inclusively, in the ear to be implanted in the preoperative aided condition and in the contralateral ear will be equal to or better than that of the ear to be implanted but not more than 80% correct. Prospective candidates should go through a suitable hearing aid trial, unless already appropriately fit with hearing aids.

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to

provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at one year. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.
In addition to the conditions outlined above, you must conduct two post-approval studies as described below:

> ***Extended Follow-up Study****:* This study is an extended follow-up of the subjects who were enrolled in the pivotal study to assess long-term device performance. The study will be conducted as a prospective, non-controlled, non-randomized, multicenter study at the 10 sites. All 39 available subjects who were enrolled in the pivotal study will be invited to participate in the extended follow-up. Study subjects will be followed for 5 years post-implantation of the device. The primary safety endpoint is the comparison of the type and frequency of adverse events and serious adverse events observed during the duration of the study compared to the pivotal study. The effectiveness endpoints will include the within-subject differences for the two speech recognition tests, i.e., word recognition in quiet as evaluated with the Consonant-Nucleus-Consonant (CNC) test, and sentence recognition in noise as evaluated with the AzBio test (+5dB SNR). The change in the perceived hearing benefits, patient satisfaction with the device use and quality of life will be assessed by employing patient reported questionnaires. Follow-up will occur at 36, 48 and 60 months post-implantation. Every explanted device will be tested to determine the reason for device failure, and device explantations will be reported as serious adverse events.

***New Enrollment Study**:* The purpose of this study is to provide longer-term data on the safety and effectiveness of the Nucleus Hybrid L24 Cochlear Implant System under general conditions of use in the postmarket environment. This study will be conducted as a prospective, non-controlled, non-randomized study in 25 clinical sites. A total of 100 subjects newly treated will be enrolled. Study subjects will be followed for 5 years post-implantation of the device with a target follow-up rate of 80% at the end of the study. The primary safety endpoint is the comparison of the type and frequency of adverse events and serious adverse events observed during the duration of the study compared to the pivotal study. The effectiveness endpoints will include the within-subject differences for the two speech recognition tests, i.e., word recognition in quiet as evaluated with the Consonant-Nucleus-Consonant (CNC) test, and sentence recognition in noise as evaluated with the AzBio test (+5dB SNR). The change in the perceived hearing benefits, patient satisfaction with the device use and quality of life will be assessed by employing patient reported questionnaires. Follow-up will occur at 3, 6, 12, 24, 36, 48 and 60 months post-implantation. Every explanted device will be tested to determine the reason for device failure, and device explantations will be reported as serious adverse events.

Additionally, the combined sample size of the two post-approval studies will provide a relatively precise estimation of proportion of the residual hearing loss at 5 years.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval studies. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Please be advised that the results from these studies should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

FDA would like to remind you that you should submit separate PAS Progress Reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Before making any change affecting the safety or effectiveness of the device, you must submit a

PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Vasant Dasika, Ph.D. at 301-796-6860.

Sincerely yours,

Christy L. Foreman -S

Christy Foreman
Director
Office of Device Evaluation
Center for Devices and Radiological Health

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Hybrid Cochlear Implant

Device Trade Name: Nucleus® Hybrid™ L24 Cochlear Implant System, consisting of:

- CI24REH Cochlear Implant
- Nucleus 6 Sound Processor (CP910 or CP920) with Acoustic Component, cable, and coil; Accessories, including CR200 Series Remote Assistants (CR210 or CR230 for patient use, CR220 for intraoperative professional use)
- Custom Sound v4 programming software

Device Procode: PGQ

Applicant's Name and Address: Cochlear Americas
13059 E Peakview Ave.
Centennial, CO 80111

Date(s) of Panel Recommendation: November 8, 2013

Premarket Approval Application (PMA) Number: P130016

Date of FDA Notice of Approval: March 20, 2014

Priority Review: Granted priority review status on June 27, 2013 because the device represents a breakthrough technology.

II. INDICATIONS FOR USE

The Nucleus® Hybrid™ L24 Cochlear Implant System is intended to provide electric stimulation to the mid- to high-frequency region of the cochlea and acoustic amplification to the low frequency regions, for patients with residual low frequency hearing sensitivity. The system is indicated for unilateral use in patients aged 18 years and older who have residual low-frequency hearing sensitivity and severe to profound high-frequency sensorineural hearing loss, and who obtain limited benefit from appropriately fit bilateral hearing aids.

Typical preoperative hearing of candidates ranges from normal to moderate hearing loss in the low frequencies (thresholds no poorer than 60 dB HL up to and including 500 Hz), with severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥75 dB HL) in the ear to be implanted, and moderately severe to

profound mid to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥ 60 dB HL) in the contralateral ear.

The CNC word recognition score will be between 10% and 60%, inclusively, in the ear to be implanted in the preoperative aided condition and in the contralateral ear will be equal to or better than that of the ear to be implanted but not more than 80% correct.

Prospective candidates should go through a suitable hearing aid trial, unless already appropriately fit with hearing aids.

III. CONTRAINDICATIONS

The device is contraindicated for individuals who have the following conditions:

1. Deafness due to lesions of the acoustic nerve or central auditory pathway
2. Active middle ear disease, with or without tympanic membrane perforation
3. Absence of cochlear development
4. A duration of severe to profound hearing loss of 30 years or greater

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Nucleus® Hybrid™ L24 Cochlear Implant System labeling.

V. DEVICE DESCRIPTION

A. General Description

The Nucleus® Hybrid™ L24 Cochlear Implant System, which is also referred to throughout this document as the Hybrid L24, is an electric-acoustic stimulation (EAS) cochlear implant system. The Hybrid L24 provides electric (cochlear implant) stimulation to the mid- to high-frequency region of the cochlea and for patients with sufficient levels of residual low-frequency hearing sensitivity postoperatively, also provides acoustic (hearing aid) amplification in low-frequency regions. It consists of both internal and external components, as illustrated in Figure 1.

Figure 1: The Nucleus Hybrid L24 Cochlear Implant System, consisting of the model Hybrid L24 Implant (top), Nucleus 6 Sound Processor with Acoustic Component (bottom left), and two Remote Assistant options, the basic CR210 (bottom middle) or the full function CR230 (bottom right). Illustrations not to scale.

B. Hybrid L24 Implant

The receiver/stimulator assembly and extracochlear electrodes of the Hybrid L24 Implant are identical to those of the marketed Cochlear Nucleus model CI24RE (Freedom™) cochlear implant. However, the intracochlear electrode array of the Hybrid L24 implant is different than the conventional electrode arrays [Straight (ST) and Contour Advance (CA)] used with Cochlear's other models of cochlear implants. While the Hybrid L24 electrode array has 22 active electrodes like Cochlear's conventional electrode arrays, it is shorter and thinner. The goal of this design is to preserve the integrity of the apical region of the cochlea (which mediates low frequencies) and thus increase the possibility of retaining a level of residual low-frequency hearing sensitivity. While conventional, longer electrode arrays marketed by Cochlear typically achieve insertion depths into the cochlea of up to 25 mm (or 420 degrees), the Hybrid L24 electrode array is designed for an insertion depth of up to 16 mm (or 270 degrees).

C. Nucleus® 6 (CP900 series) Sound Processor

The Nucleus® 6 Sound Processor (i.e., CP900 series of sound processor) includes an Acoustic Component that can provide conventional amplification for residual acoustic hearing sensitivity in the lower frequencies. Two versions of the Nucleus 6 sound processor are available: the CP910 and the CP920. These sound processors are identical except that the CP920 has an accessory port for use with accessories.

Both the electric (cochlear implant) and acoustic (hearing aid) sound processing are programmed using Custom Sound Suite software, version 4. Two remote controls are available for patient use: the CR210 basic Remote Assistant and the CR230 fully-featured Remote Assistant. A third remote control is also available only for use by professionals in the operating room, the CR220 Intraoperative Remote Assistant.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The most common alternative treatment of severe to profound bilateral high-frequency sensorineural hearing loss with residual low-frequency hearing is the use of conventional air conduction hearing aids or, in some cases, frequency transposition hearing aids. Patients may also choose to forego obtaining a hearing device and pursue rehabilitation via speechreading and/or sign language training. Each of these alternatives has its own advantages and disadvantages. A patient should fully discuss the alternatives with his/her physician and audiologist in order to select the treatment that best meets his/her expectations and lifestyle.

VII. MARKETING HISTORY

The Hybrid L24 has been marketed for use in both adults and children in the following countries: Algeria, Argentina, Australia, Belarus, Belgium, Bolivia, Canada, Columbia, Czech Republic, Egypt, Finland, France, Germany, Hong Kong, Hungary, Iran, Israel, Italy, Korea, Malaysia, Netherlands, New Zealand, Norway, Poland, Russian Federation, Saudi Arabia, Singapore, Slovenia, Spain, Sweden, Switzerland, Turkey, and United Kingdom. Since market introduction, approximately 315 Hybrid L24 systems have been implanted worldwide. The Hybrid L24 has not been withdrawn from any market for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects/complications associated with the implantation and use of the Hybrid L24:

- Sudden losses of residual low-frequency hearing
- Total loss of residual hearing

- Vertigo, dizziness, or balance problems that did not exist preoperatively or worsened postoperatively
- Facial nerve problems including injury and unintended stimulation
- Meningitis
- Perilymphatic fistulae
- Tinnitus that did not exist preoperatively or worsened postoperatively
- Implant Migration/Extrusion
- Skin flap problems
- Device-related problems including programming problems and device failure requiring explantation/reimplantation.

For the specific adverse events that occurred as part of the clinical study, see Section X.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Intracochlear Electrode Array

Table 1 summarizes the preclinical testing conducted for the intracochlear electrode array and lead, including information about the test, purpose, acceptance criteria and results.

Table 1. Intracochlear electrode array and lead testing

Test	Purpose	Acceptance Criteria	Results
Temporal bone insertion	To assess the insertion trauma and performance characteristics of the Hybrid L24 electrode	Verify that the insertion characteristics and insertion safety are acceptable for human implantation in a controlled clinical trial	Electrodes inserted into 18 temporal bones by experienced otologic surgeons using a standard posterior tympanotomy approach. Histological assessment of the temporal bones showed no evidence of trauma. Results also showed minimal resistance when inserting the electrode, full insertion depth could be achieved with a single stroke insertion, and the electrode did not buckle in the proximal region.
Multiple insertion Testing	The electrode array is repeatedly inserted into a model cochlea to ensure sufficient robustness to withstand the forces exerted during manufacture and implantation	Equivalent or better Mechanical and electrical reliability criteria when compared to current approved electrode after 50 insertion and removal cycles	5 Hybrid L24 electrode arrays were tested and passed acceptance criteria
Linear and angular fatigue test of the electrode array	To demonstrate that implant leads have the required resistance to fatigue	Samples must survive 2.5 million cycles while maintaining continuity and showing no visible signs of damage	A total of 12 units were exercised through +/- 30º angular (four units) and +/- 10% of electrode length (eight units) at about 2 cycles per second, in a number of different test planes. All samples met acceptance criteria
Severe stress and twist of the electrode lead	To ensure the electrodes will withstand severe stress caused by stretching, and twisting	Implant must maintain electrical continuity throughout testing process, visual inspection must show no signs of damage	Two electrode leads were stretched by 10% and rotated 360º clockwise and 360º counter-clockwise over 10 cycles. All samples met acceptance criteria

Test	Purpose	Acceptance Criteria	Results
Severe electrode lead shear test	To ensure the electrodes will withstand severe stress caused by shearing	Implant must maintain electrical continuity throughout testing process, visual inspection must show no sign of damage	Two electrodes leads were clamped at a 90º angle to the longitudinal axis of the implant (all four possible orientations were tested). The face of the shear tool was placed perpendicular to the electrode lead at a distance of 1.2 mm from the titanium case. Electrical continuity of the lead was monitored while the shear tool was pushed slowly (0.1mm/s) to the lead. All samples met acceptance criteria

Preclinical Safety Analysis:
Charge density calculations were performed to specify safe stimulus current levels for the Hybrid L24 implant. Taking into account the area and periphery of the smallest electrode surface, charge density calculations were completed to assure safe current stimulation by electrodes in the cochlea.

B. External Components

Mechanical Robustness and Environmental Testing of External Components
Mechanical and environmental testing was conducted on the external components and remote assistants. This testing is summarized in Table 2:

Table 2. Mechanical robustness and environmental testing of CP900 series of sound processor and remote controls

Test	Purpose	Acceptance Criteria	Results
Cold test	To ensure units can withstand ambient temperatures (-40°C ± 3°C) the product has the possibility of experiencing during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	The units were exposed to conditions specified in IEC 60068-2-1 Part 2 Test Ab: Starting Temperature: Ambient; Rate of Change: <1°C/min (Averaged over 5 min); Test Temperature: -40°C ± 3°C for 16 hours. All units met acceptance criteria
Dry heat	To ensure units can withstand ambient temperatures (70°C ± 3°C) the product has the possibility of experiencing during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	The units were exposed to conditions specified in IEC 60068-2-1 Part 2 Test Bb: Starting Temperature: Ambient; Rate of Change: <1°C/min (Averaged over 5 min) worksheet to record rate; Test Temperature: +70°C ± 2°C for 16 hours. All units met acceptance criteria
Thermal cycling	To ensure units can withstand shifts in temperature (-40°C to 70°C at 1°C ± 0.2°C /min) the product has the possibility of experiencing during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	The units were exposed to conditions specified in IEC 60068-2-1 Part 2 Test Nb: Temperature Range: -40°C to 70°C; Rate of Change: 1°C ± 0.2°C/min; Number of Cycles: 2; Exposure Time at Endpoints: 3 hours per cycle. All units met acceptance criteria
Cyclic damp	To ensure units can withstand environmental conditions (55°C ± 2°C, 93±3% RH, then 25°C ± 3°C, 95% RH) the product has the possibility of experiencing during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	Samples were exposed to conditions specified in IEC 60068-2-1 Part 2 Test Dd: 55°C ± 2°C, 93±3% RH, for 12 hours, then 25°C ± 3°C, 95% RH, for 12 hours and repeated for a total of 6 cycles. All samples met acceptance criteria

Test	Purpose	Acceptance Criteria	Results
Low pressure	To ensure units can withstand low pressures (100 hPa ± 5 %) the product has the possibility of experiencing during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	Samples were placed in a pressure chamber set at 100 hPa (7.25 psi) ± 5 % for 1 hour with no significant damage noted. All samples met acceptance criteria
Random vibration	To ensure units can withstand mechanical strain in the form of random vibration (frequency bandwidth of 5 to 150Hz) as could be expected during field use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	Samples were subjected to random vibration (BS EN 45502-1:1998, Section 23.2 as per IEC 60068-2-64 Ed. 2.0 b:2008, Test Fh) at a frequency bandwidth of 5 to 150 Hz at an accelerated spectral density of $0.1g^2$/Hz for 30 minutes, across three orthogonal planes. All samples met acceptance criteria
Free fall	To ensure unit can sustain rough shocks that could result from a fall, with three drops at 2.0m being the worst case scenario of normal use	All devices must show neither mechanical damage nor degradation in electrical functionality after testing	Samples were subjected to a free fall drop test (EN 45502-2-3:2010, Section 23.1 as per IEC 60068-2-31 Ed. 2.0, 2008-05, Test Ec). The case half of one CP910 Standard Sound Processor cracked during Freefall testing, and the sound processor remained fully functional. All other tested units showed no cracking and remained fully functional
Ingress protection testing (external components only)	To ensure the unit can resist ingress of solid foreign objects (≥1mm), splashing of liquid (50 kPa – 150 kPa), and dust (<75µm)	All units must be free of evidence of ingress of the test material	IP44 testing was conducted per IEC 60529 Ed. 2.1 b:2001. All configurations passed the testing. IP57 testing was conducted using the rechargeable battery pack per IEC 60529 Ed. 2.1 b:2001. All configurations of units passed IP44 and IP57 ingress protection testing

Test	Purpose	Acceptance Criteria	Results
Clamp force	To assess the ability of the earhook to resist a biting action without producing loose parts or sharp points	The biting action shall not produce any sharp parts or points. It also must not sever the ear hook to produce loose parts	External retention components were subjected to a test using a bite test clamp positioned in an Instron force tester. The force was gradually increased from 0 at a rate of 10N per second until the bite force reached 140N, and held for 5 seconds.All samples met acceptance criteria
Overmould strength test	To assess the strength of the overmould on external retention devices	Force required to delamination the soft part of the earhook from the hard part is greater than 30N	Using a test jig and an Instron force tester, the strength of the overmould on external retention devices was analyzed by increasing force using a displacement rate of 1mm per second. Acceptance criteria were met and the maximum force reached during delamination of parts was greater than 30N
Retention tests	To ensure adequate retention strength of the small CI earhook and small snugfit with band	The force required to remove all units must be greater than 22.5N.	Several tests were set up to measure the force it takes to detach retention components. Acceptance criteria were met and the test subject was only detached with a force >22.5N
LED light test	To ensure the LED light of the external sound processor is visible in expected indoor conditions	BTE under test must be visible from a distance equal to or larger than 4m in an office environment, when looking directly at the BTE	A light meter was used to measure sound processor LED alert light levels. Acceptance criteria were met and light levels were maintained between 100 and 1500 lux

Electrical Testing of CP900 series sound processor

Electrical testing was conducted on the CP900 series sound processor. This testing is summarized in Table 3:

Table 3. Electrical testing of CP900 series sound processors

Test	Purpose	Acceptance Criteria	Results
Electrical basic functionality	To assess typical electrical functionality, including button operation, LED function, voltage / current measurements, audio input channels, and audio output measures	Electrical functions perform as intended, and operate within prescribed voltage / current / resistance windows	Verification testing demonstrated that the general electronic hardware of the remote assistants functions in the manner intended. All acceptance criteria have been met.
RF link electrical verification	To verify performance of the RF link between the CP900 processor and Cochlear implant. This includes RF link coverage, RF link efficiency, and RF link data integrity	All link measurements must fall into specified ranges representing worst case conditions	All units tested met acceptance criteria, with a deviation of one test configuration. The fault in this configuration would manifest as intermittency, and is resolvable through reprogramming
Mobile phone compatibility and RF immunity	To verify the compatibility of the CP900 Sound Processor with use in close proximity to hand held mobile phones, DECT wireless phones and other devices that emit RF radiation	All sound processor configuration must meet requirements for user compatibility and immunity levels as defined by ANSI standard C63.19	The units tested complied with all immunity requirements
Radio testing	Demonstrate that the components of the Nucleus 6 system that are radio frequency radiators meet the Radio regulations and standards required in the United States and other countries.	Using configurations that are representative of the typical system usage, show that no harmful interference is caused.	Verification testing demonstrated that the CP900 series sound processor meets the radio regulations (47 CFR Part 15, RSS – 210 issue 8, EN 300 328 as per R&TTE Directive 199/5EC and CEPT/ERC 70-03). Remote assistants function with firmware as intended, no harmful interference is caused.

Test	Purpose	Acceptance Criteria	Results
EMC (Electromagnetic Compatibility)	To verify that the Sound Processor satisfies requirements for electromagnetic compatibility in clinical use	Meet several criteria for both emissions and immunity (see Results column)	Verification testing demonstrated that CP900 Series meets EMC requirements: Radiated Emissions (CISPR 11), Electrostatic Discharge (IEC 61000-4-2), Radiated RF Field (IEC 61000-4-3), Conducted RF Disturbances (IEC 61000-4-6), Power Frequency Magnetic Field (IEC 61000-4-8), and Immunity (EN 45502-2-3 Clause 27.2 and Clause 27.3), Immunity of Hearing Aids to interferences generated by a wireless phone (IEC60118-13:2011)
RF Link Wireless Range	Verify the wireless range between the external sound processor and the internal device, in both microphone and telecoil modes	To deliver appropriate voltage for skin flap thicknesses between 1mm and 10mm	The units tested complied with acceptance criteria and all wireless range requirements

Electrical Testing of Remote Assistants

Electrical testing was also conducted on the various remote assistants. This testing is summarized in Table 4:

Table 4. Electrical testing of remote assistants

Test	Purpose	Acceptance Criteria	Results
Basic functionality (CR210 / CR230)	To verify the electronic hardware of CR200 series Remote Assistants and show compliance of the devices with the relevant system and electrical component requirements	Considered to pass only if all of the discrete/attribute- based measurements for every tested sample achieve a pass.	Verification testing demonstrated that the general electronic hardware of the remote assistants functions in the manner intended. All acceptance criteria have been met.
EMC (Electromagnetic Compatibility: Radiated Emissions) (CR210 / CR230)	To verify that the Remote Assistant satisfies requirements for Radiated Emissions in clinical case.	Meet the Radiated Emission requirements as per CISPR11[E2].	Acceptance criteria were met. Verification testing demonstrated that the remote assistants meet CISPR11[E2].
EMC: Wireless link, immunity to RF (CR220)	To ensure that the CR220 Intraoperative Remote Assistant will operate as intended in an operating room, when subjected to external interference.	While subjected to interference levels: 1. CR220 shall not be permanently damaged 2. The Sound Processor and/or CR220 can power down and be repowered 3. CR220 shall display RF link loss 4. Impedance or NRT measurement shall not automatically resume with the link auto reconnect.	Verification testing demonstrated accordance to IEC61000-4-3 procedure with a 20V/m level to simulate anticipated interference in a surgical operating theatre. The CR220 Intraoperative Remote Assistant complied with immunity requirements and met acceptance criteria.
Wireless Range Verification (CR210 / CR230)	Verify the wireless range between the external sound processor and Remote Assistant.	At least 80% (40 out of 50) command attempts are successful at a distance of 2m (+/- 5cm) at a variety of angles	The remote assistant met acceptance criteria

Test	Purpose	Acceptance Criteria	Results
Radio compliance (CR210 / CR230)	Demonstrate that the components of the Nucleus 6 system that are radio frequency radiators meet the Radio regulations and standards required in the United States and other countries.	Using configurations that are representative of the typical system usage show that no harmful interference is caused.	Remote assistants function with firmware as intended, no harmful interference is caused.

Lithium Ion battery testing for CP900 series sound processor

Battery safety testing was conducted for the two rechargeable lithium ion batteries that are available for the CP900 series sound processor. These two batteries are offered with the Hybrid L24. This testing is summarized in Table 5:

Table 5. Lithium Ion Battery testing

Test	Purpose	Acceptance Criteria	Results
Testing of rechargeable batteries to UL 1642	To validate the standards that the lithium ion battery applies in the following tests:	See subtest acceptance criteria below	Acceptance criteria were met for all UL1642 tests.
UL 1642: Short circuit at room temperature	To test the discharge response of the battery when charged cells had a short circuit	Units did not explode, catch fire, or rupture during testing. The temperature of the cell did not exceed 150°C.	Units did not explode, catch fire, or rupture during testing and the temperature was within acceptable limits.
UL1642: Short Circuit at 55 °C	To test the discharge response of the battery when charged cells had a short circuit in a warm environment	Units did not explode, catch fire, or rupture during testing. The temperature of the cell did not exceed 150°C.	Units did not explode, catch fire, or rupture during testing and the temperature was within acceptable limits.
UL1642: Abnormal Charge	To evaluate the response of the battery when the cells were charged with maximum specified charge voltage and a current limit of three times the specified maximum current.	Units did not explode, catch fire, or rupture during testing.	Units were intact following the testing.

Test	Purpose	Acceptance Criteria	Results
UL1642: Crush	To test the response of the battery cells under an applied force of 13 ±1kN (3000 ±224 pounds).	The samples did not explode or catch fire.	Units sustained some damage, but met acceptance criteria.
UL1642: Impact	To evaluate the response of the cells after a 20 pound weight was dropped from a height of 24 inches onto the sample.	The units did not explode or catch fire.	Units sustained some damage, but met acceptance criteria
UL1642: Shock	To evaluate the response of the cells after exposure to three shocks of equal magnitude.	The units did not explode, catch fire, leak or vent.	Units did not have any weight change, and met acceptance Criteria
UL1642: Vibration	To evaluate the response of the battery cells after exposure to vibration testing on each of three axes for not less than 90 minutes nor more than 100 minutes.	The units did not explode, catch fire, leak or vent.	Units did not have any weight change, and met acceptance criteria
UL1642: Heating	To measure the response of the cells after with an initial temperature of 20 ± 5ºC (68 ±9ºF), increasing to 130 ± 2°C (266 ± 3.6°F).	The units did not explode or catch fire.	Cells did not explode or catch fire in extreme heat.
UL1642: Temperature cycling	To evaluate the response of fully charged cells subject to hot and cold temperatures in succession.	The units did not explode, catch fire, vent, or leak.	Units did not have any weight change, and met acceptance criteria.

Test	Purpose	Acceptance Criteria	Results
UL1642: Projectile	To measure whether the battery would penetrate a metal screen (a single layer of 0.25 mm diameter wire with 16-18 wires per inch in each direction) when heated until the point it exploded.	Units did not penetrate wire screen.	Units did not penetrate the wire screen and met acceptance criteria.
UL1642: Altitude	To evaluate how a fully charged cell would react when stored for 6 hours at an absolute pressure of 11.6 kPa (1.68 PSI) and a temperature of 20 ± 3° C (68 ± 5° F).	The units did not explode, catch fire, vent, or leak.	Units did not have any weight change, and met acceptance criteria.
Testing of rechargeable batteries to IEC 62133	To validate the standards that the lithium ion battery applies in the following tests:	See subtest acceptance criteria below	Acceptance criteria were met for all IEC 62133 tests.
IEC62133: Insulation and wiring	To evaluate the characteristics of insulation and wiring, including: insulation resistance, maximum anticipated current / voltage / temperature requirements, and wiring orientation / integrity	Insulation resistance was evaluated and is greater than 5MΩ, no internal wiring is compromised due to current / voltage / temperature, and internal connections are sufficient despite reasonable foreseeable misuse	Acceptance criteria were met for all tests
IEC62133: Vibration	To evaluate the response of the battery cells after exposure to vibration testing on each of three axes for 90 minutes ± 5 minutes for each mounting position	The units must not explode, catch fire, leak or vent, and measured open circuit voltage must be within anticipated parameters	Units did not have any weight change, and met acceptance criteria
IEC62133: Moulded case stress at high temperature	To assess the moulded case at high ambient temperature of 70°C ± 2°C for seven hours	A lack of physical distortion of the battery casing, or exposure of internal components	No physical distortion of battery casing was present

Test	Purpose	Acceptance Criteria	Results
IEC62133: Temperature cycling	To evaluate resistance to change in temperature (-20°C to 75°C)	A lack of physical distortion of the battery casing, or exposure of internal components, including fire, explosion, or leakage	No physical distortion of battery casing was present, including fire, explosion, or leakage
IEC62133: External short circuit	To evaluate the resistance of battery cells to an external short circuit at 20°C ± 5°C and at 55°C ±5°C	The units must not exceed an external resistance of 100mΩ, and the units must show no leakage, fire, or explosion	Units met acceptance criteria including a lack of leakage, fire, or explosion
IEC62133: Free Fall	To assess the ability of battery cells to resist an impact from a height of 1.0m onto a concrete surface	The units must not explode or catch fire	All units met acceptance criteria
IEC62133: Mechanical Shock (Crash Hazard)	To evaluate the resistance of battery cells to a total of three shocks of equal magnitude applies in three mutually perpendicular directions	A lack of physical failure, including fire, explosion, or leakage	Units met acceptance criteria including a lack of fire, explosion, or leakage

C. Hybrid L24 End to End Acoustic Verification Testing

End-to-end testing including electrical and acoustical verification, acoustical system behavior and listening tests were completed to verify that the Hybrid L24 functions as intended. Some acceptance criteria have not been met. Two issues occur only at a very high sound level and at a specific frequency (750Hz). Both issues are therefore deemed by the applicant to be acceptable for clinical use as they do not impact the safety and effectiveness of the system. Overall, the results demonstrate that the system functions as intended.

D. Biocompatibility

Intracochlear Electrode Array:
All materials used in the Hybrid L24 electrode array are identical to those used in the CI24RE series introcochlear electrode arrays. The manufacturing process is also unchanged, along with the facilities used, such as cleanrooms, sterilization tools, and sealing machines. Given the changes in design have resulted in no change to manufacturing materials, processes, or equipment, biocompatibility testing performed on the CI24RE series implants may be applied to the Hybrid L24 implant and is summarized below:

Cytotoxicity
Cytotoxicity testing was conducted on prior generation implants to ISO10993-5:1999 and any differences with the latest version (ISO 10993-5:2009) were adequately justified.

Sensitization
Sensitization testing was conducted on prior generation implants to ISO 10993-10:1995 and any differences with the latest version (ISO10993-10:2010) were adequately justified.

Irritation or Intracutaneous Reactivity
Intracutaneous Reactivity testing was conducted on prior generation implants to ISO 10993-10:1995 and any differences with the latest version (ISO 10993-10:2010) were adequately justified.

Systemic Toxicity (acute)
System Toxicity testing was conducted on prior generation implants to ISO 10993-11:2006.

Subacute and Subchronic Toxicity
Subacute and Subchronic Toxicity testing was conducted on prior generation implants to ISO 10993-11:2006.

Genotoxicity
Genotoxicity testing was conducted on prior generation implants to ISO 10993-3:1992 and any differences with the latest version (ISO10993-3:2003) were adequately justified.

Implantation
Implantation testing conducted on prior generation implants to ISO 10993-6:1994 and any differences with the latest version (ISO10993-6:2007) were adequately justified.

CP900 External Components and Remote Assistants:
Testing should indicate materials are non-sensitizing, non- irritation, and no toxicity for all materials with some degree of skin contact in the CP900 System. Biological evaluations/tests were conducted according to ISO 10993-5 and ISO 10993-10. No failures were observed. The materials contained within the CP900 system are therefore safe for use.

E. Sterilization

The Hybrid L24 implant has been adopted into Cochlear's validated EtO Sterilization Process according to AAMI TIR28:2009, therefore demonstrating compliance with EN556-1:2001, ISO 11135-1:2007, ETO residual safety per ISO10993-7:2008 and the requirements for medical device packaging per ISO11607-1:2006. Package validation testing is summarized in Table 6.

Table 6. Package validation testing

<table>
<tr><th>Test Name</th><th>Standard Utilized</th><th>Acceptance Criteria</th></tr>
<tr><td>Visual Inspection</td><td>ASTM F1886</td><td>The package has a complete seal per the following table:
<table>
<tr><th>Package Type</th><th>Minimum seal width requirements</th></tr>
<tr><td>Sterile barrier family #1</td><td>Seal Width ≥ 4.9mm</td></tr>
</table>
When using a bench-top illuminated magnifier lamp, there are no cracks, crevices or tracks in any direction in the seal longer than 2mm.
Without magnification, there is no warping or other visual damage to the tray.
There are no irregularities on the inside surfaces of the TYVEK lid, including tears, cracks, holes or fractures.</td></tr>
<tr><td>Peel Strength</td><td>ASTM F88</td><td>The peak force measured for each sample shall be equal to or above 5.5 N.</td></tr>
<tr><td>Dye Penetration</td><td>ASTM F1929</td><td>Visual inspection of the seal region of tested packages shall show no evidence of dye penetration to the opposite side of the seal via a defined channel, indicating the presence of a leakage site.
Evidence of dye penetration through the porous material through general wetting of the surface (wicking) shall not be taken as the indication of the presence of a leakage site.</td></tr>
<tr><td>Burst Strength</td><td>ASTM F1140</td><td>
<table>
<tr><th>Package Component</th><th>Minimum Burst Pressure (kPa) Before Package Failure</th></tr>
<tr><td>Inner</td><td rowspan="2">≥ 3.7 kPa</td></tr>
<tr><td>Outer</td></tr>
</table>
</td></tr>
<tr><td>Creep</td><td>ASTM F1140</td><td>
<table>
<tr><th>Package Component</th><th>Minimum Hold Pressure (kPa) Without Package Failure</th></tr>
<tr><td>Inner / Outer</td><td>75-85% of the lowest burst test value</td></tr>
</table>
</td></tr>
<tr><td>Sterility</td><td>ISO 11737-2:2009</td><td>No Growth</td></tr>
<tr><td>Smudge test</td><td>ASTM F2250</td><td>No smudging shall be visible on any of the samples following the test.</td></tr>
</table>

Shelf Life:

Expiration dating for the Hybrid L24 has been validated through both accelerated aging and real-time aging. Accelerated aging was performed according to ASTM F 1980-2007 to an equivalent of 2.5 years, and real-time aging was performed to one year. Following aging, the test articles were subjected to the tests identified in Table 6 above. As real-time aging results were not available for time points later than 2 years, a shelf life of one year has been established for the device, and will be indicated on the labeling.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant conducted a clinical study to establish reasonable assurance of safety and effectiveness of the Hybrid L24 in subjects 18 years an older in the US under IDE G070191. Data from this clinical study were the basis for the PMA approval decision. In addition, the applicant has conducted two earlier clinical studies outside of the US on the Hybrid L24 which are briefly described below.

Outside US studies of Hybrid L24

In 2005, a study of the Hybrid L24 was initiated by the applicant in Australia at a single site. Thirteen subjects were implanted and one withdrew following device activation due to advancing Alzheimer's disease symptoms. Group mean word recognition scores reportedly improved. Three of the twelve continuing subjects (25%) experienced low-frequency threshold shifts that exceeded 30 dB at 12 months, while the remaining 9 subjects had smaller threshold shifts.

In 2006, the applicant initiated a multicenter study in the European Union to support its application for the CE mark of the Hybrid L24. There were 16 study sites; 66 subjects were enrolled and implanted. While the collection of effectiveness measures (e.g., speech recognition scores, speech reception thresholds) differed across study sites, speech recognition in quiet was tested most commonly tested and improvements in this measure were generally reported. The group mean for the low-frequency threshold average worsened by 15.1 dB at 6 months post-implantation.

A. Study Design

The pivotal study for the Hybrid L24 was conducted under IDE to evaluate the safety and effectiveness of the Hybrid L24 in individuals who demonstrate significant residual low-frequency hearing and profound high-frequency (above 1500 Hz) sensorineural hearing loss.

The study was a prospective, multi-center, one-arm, non-randomized, non-blinded, repeated-measures clinical study. Both objective and subjective performance data were collected. Each subject served as her or his own control so that post-implant performance was compared to each subject's baseline (pre-implant) performance. Fifty subjects were implanted with a Hybrid L24 across 10 investigational sites.

Investigational Sites

The following list identifies the 10 investigational sites (all US sites); the number of subjects enrolled at each site is identified in parentheses:

- Midwest Ear Institute in Kansas City, Missouri (11)
- NYU Medical Center in New York, New York (10)
- Mayo Clinic in Rochester, Minnesota (7)
- Hearts for Hearing in Oklahoma City, Oklahoma (6)
- Northwestern University in Chicago, Illinois (3)
- Ohio State University in Columbus, Ohio (3)
- Rocky Mountain Ear Center in Denver, Colorado (3)
- University of Cincinnati in Cincinnati, Ohio (3)
- University of Iowa in Iowa City, Iowa (3)
- Center for Hearing and Balance in Chesterfield, Missouri (1)

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in G070191 was limited to patients who met the following inclusion criteria:

   - 18 years of age or older at the time of implantation
   - Severe to profound sensorineural hearing loss for frequencies > 1500 Hz (i.e., threshold average at 2000, 3000, & 4000 Hz > 75dB HL). Low-frequency thresholds up to and including 500 Hz should be no poorer than 60 dB HL
   - CNC word recognition score (mean of two lists) between 10% and 60%, inclusive (i.e., 10% < score < 60%), in the ear to be implanted
   - CNC word recognition score in the contralateral ear equal to, or better than, the ear to be implanted but not more than 80%
   - English spoken as a primary language

   Patients were excluded from the study if they met any of the following exclusion criteria:

   - Duration of severe-to-profound hearing loss greater than 30 years
   - Congenital hearing loss (for the purpose of this study, onset prior to 2 years of age)
   - Medical or psychological conditions that contraindicate undergoing surgery
   - Ossification or any other cochlear anomaly that might prevent complete insertion of the electrode array
   - Conductive overlay of 15 dB or greater at two or more frequencies, from 250 to 1000 Hz
   - Hearing loss of neural or central origin
   - Diagnosis of Auditory Neuropathy
   - Active middle ear infection
   - Unrealistic expectations on the part of the subject, regarding the possible benefits, risks, and limitations that are inherent to the surgical procedure(s) and prosthetic devices

- Unwillingness or inability of the candidate to comply with all investigational requirements

2. Follow-up Schedule

This study involved up to nine visits before and after implantation, for about a one-year period. Candidacy testing included medical and audiological evaluations to determine study eligibility. A 2-week hearing aid trial was required for those prospective subjects who were not previous users of hearing aids that were determined as fit appropriately prior to being accepted as a study candidate, which required one or two additional visits. After confirming eligibility, the subject underwent baseline testing. The device was subsequently implanted in one ear in accordance with the subject candidacy criteria. The device was activated following a healing period of 2 to 4 weeks.

The baseline and postoperative measurements are summarized in Table 7. All patients were scheduled to return for follow-up examinations at 3, 6, and 12 months postoperatively. Preoperatively, a baseline evaluation was conducted that included collection of both unaided and hearing-aided threshold measures, and also hearing-aided baseline measures for the two co-primary effectiveness endpoints (CNC words and AzBio sentences). Postoperatively, the objective parameters measured included the effectiveness endpoint measures under various testing conditions (described below Table 8). Adverse events and complications were recorded at all visits.

Table 7: Schedule of study visits[1]

	Baseline Evaluation	Initial Device Activation	3-month Postoperative	6-month Postoperative	12-month Postoperative
Informed Consent	X				
Medical and Hearing History	X				
Verification of Hearing Aid functioning	X		X	X	X
Unaided Hearing Thresholds and Tympanometry	X	X	X	X	X
Aided Audiometric Thresholds	X	X	X*	X*	X*

	Baseline Evaluation	Initial Device Activation	3-month Postoperative	6-month Postoperative	12-month Postoperative
Aided CNC test in quiet	X		X	X	X
Aided AzBio sentences-in-noise test	X		X	X	X
Adaptive SRT in noise	X			X	
Aided UW-CAMP music perception	X			X	
Questionnaires (SSQ, DUQ, MBQ)	X			X	X
Psychophysical Ts and Cs and electrical impedance		X	X	X	X
Adverse event reporting	X	X	X	X	X

[1] Subjects continued to be monitored on a semi-annual basis after the 12-month interval until study closure. *Aided thresholds were only retested if there was a change in unaided hearing sensitivity at that interval compared to the previous interval.

3. Clinical Endpoints

Test Conditions

Five pre- or post-implant test conditions were proposed: Acoustic Alone (acoustic stimulation to the ear to be implanted), Bilateral Acoustic (acoustic stimulation to both ears), Hybrid (simultaneous electric and acoustic stimulation in the implanted ear via the Hybrid L24 including the Acoustic Component), Bimodal (electric stimulation only using the Hybrid L24 minus the Acoustic Component with contralateral acoustic stimulation), and Combined (electric and acoustic stimulation via the Hybrid L24 and contralateral acoustic stimulation).

Postoperatively, there were three major conditions: Hybrid, Bimodal and Combined, which are illustrated in Table 8 below. The Bimodal condition refers to listening via electrical stimulation to implanted ear and acoustic amplification to the other ear, while the Combined condition refers to listening via electrical stimulation to the implanted ear, along with bilateral acoustic amplification. In the applicant's labeling, the results from the Bimodal and Combined conditions were collapsed and these two conditions were collectively referred to as "Everyday Listening". In order to maintain consistency with the applicant's labeling, the

term “Everyday Listening” is similarly adopted in the remainder of this SSED to describe these two test conditions. The term “Everyday Listening” was not defined as part of the test conditions in the applicant’s study protocol.

Table 8: Postoperative Test Conditions

Condition		*Everyday Listening*	
	*Hybrid**	*Bimodal*	*Combined*
Description	Electrical stimulation and acoustic amplification (HA) to the implanted ear	Electrical stimulation to implanted ear and acoustic amplification to the other ear	Acoustic amplification bilaterally, plus electrical stimulation to the implanted ear
			

* For those subjects who developed a profound /total loss of residual low-frequency hearing, the applicant performed testing with the Hybrid L24 without the Acoustic Component (i.e., electric-alone mode) and included these data under the “Hybrid” condition.

Endpoints

Safety Endpoint: The primary safety endpoint was the number and proportion of individuals experiencing an adverse event, defined as any surgical and/or device-related event. The adverse events include anticipated and unanticipated adverse events. The list of anticipated adverse device effects identified by the applicant follows:

1. Sudden changes in residual low-frequency hearing.
2. Total loss of residual hearing.
3. Vertigo, dizziness, or balance problems that did not exist preoperatively or worsened postoperatively.
4. Facial nerve problems.
5. Meningitis.
6. Perilymphatic fistulae.
7. Tinnitus that did not exist preoperatively or worsened postoperatively.
8. Implant Migration/Extrusion.
9. Skin flap problems.
10. Device-related/programming problems.

The applicant did not propose formal statistical hypothesis testing for the safety endpoint.

Co-Primary Effectiveness Endpoints: Two co-primary effectiveness endpoints were proposed: CNC word-recognition scores and AzBio sentence-in-noise scores. The score for each metric was compared across two conditions: the

(baseline) Acoustic Alone condition and the 6-month postactivation Hybrid condition.

Study success was defined as a statistically significant improvement ($\alpha = .05$) in both co-primary endpoint measures. The null hypothesis (H_0) and alternative hypothesis (H_A) were defined as follows:

H_0: Mean improvement ≤ 0.

H_A: Mean improvement > 0.

Each hypothesis was tested using a paired t-test with one-sided significance level of 0.025. If there was significant evidence that the assumptions of the t-test did not hold (i.e., $p<0.05$ from a Shapiro-Wilk test of normality), a Wilcoxon signed rank test was used.

The consistency of the primary endpoints was examined across investigational sites by testing for an effect of site in an ANOVA model.

Missing 6-month postactivation data were proposed to be imputed using the last observation carried forward (LOCF) approach.

Sample Size

The calculated minimum sample size was 47 subjects, and the final proposed sample size was 50. With the sample size, the study had more than 90% power to detect 18.1% improvement in the mean CNC word scores and 12% improvement in the mean AzBio sentence-in-noise scores. The effect sizes for these endpoints were based on clinical trial data from a previous Hybrid IDE study (G990155).

Secondary Effectiveness Endpoints: Secondary effectiveness endpoints compared 6-month post-operative performance in the Hybrid condition to preoperative (ipsilateral) Acoustic Alone performance. Three secondary endpoints were defined as the proportion of subjects scoring equal to or better on the following measures: CNC words, CNC phonemes, and AzBio sentences. The success criteria was greater than 75% of subjects for each secondary endpoint. No statistical hypothesis testing was proposed for these secondary effectiveness endpoints.

Audiometric Test Methods & Effectiveness Measures

Audiometric Thresholds

Unaided audiometric thresholds were obtained for each ear, with insert earphones, using the standard audiometric technique for pure-tone testing. Aided audiometric thresholds were obtained for each ear in the sound-field using narrow band noise

and the standard audiometric technique with the speakers positioned at 0° azimuth relative to the subject's head. The contralateral ear was masked/plugged during aided testing.

Unaided testing for both ears included air conduction thresholds at 125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz, and bone conduction thresholds at 125, 250, 500, 750, 1000, 1500, 2000, and 4000 Hz. Aided thresholds were measured at the following frequencies: 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz.

The low-frequency hearing threshold was defined as the threshold averaged over the range 125 through 1000 Hz, inclusively, in the implanted ear.

For the purposes of adverse event reporting, any change in the low-frequency hearing threshold that resulted in a profound loss (> 90 dB HL) and possibly also total loss (defined as no measurable hearing at the maximum output of the audiometer) in the implanted ear was considered by the applicant as an anticipated adverse event. All cases of profound/total loss of residual low-frequency hearing were included in the adverse event tabulations and analyses.

Effectiveness Measures

Consonant-Nucleus-Consonant (CNC) Word Recognition Test

The CNC Word Recognition Test (Peterson & Lehiste, 1962) is a psychometrically validated test of open set word recognition to determine speech intelligibility in listeners with hearing impairments. This test is consisted of 10 recorded lists of 50 monosyllabic words. At each test interval, two lists were administered in quiet at 60 dBA in the sound field and scored as percent correct for words and phonemes. Subjects were tested using a configuration where the target speech was presented via a loudspeaker at 0º azimuth.

AzBio Sentences in Noise Test

The AzBio Sentence-in-Noise Test (Spahr et al., 2012) is a psychometrically validated test to assess CI recipients' ability to understand sentences in the presence of background noise. This test consisted of 33 lists of 20 sentences (five sentences from each of two male and two female speakers. At each test interval, two lists of the AzBio sentences were presented at 60 dBA with the competing noise (multi-talker babble) at 55 dBA, to achieve a +5 dB signal-to-noise ratio. Stimuli were presented from a single loudspeaker located at 0º azimuth.

B. Accountability of PMA Cohort

A total of 100 subjects were consented to be evaluated for participation in the study. Of these 100 subjects,

- 22 failed, not meeting study requirements
- 28 were potential candidates, but discontinued participation and did not proceed with implantation. Of these 28:
    - 16 could not secure insurance and withdrew
    - 8 elected to pursue other options (nonsurgical or traditional cochlear implantation). Of these 8:
        - 3 pursued hearing aid amplification
        - 3 were either no longer interested in pursuing a surgical procedure) or had concerns regarding loss of residual hearing,
        - 2 pursued traditional cochlear implantation
    - 4 did not proceed with the surgery because the maximum number of subjects approved for implantation had been met
- The remaining 50 subjects were implanted with the Hybrid L24 implant.

Of the 50 subjects who were enrolled and implanted (all implanted unilaterally), all subjects had their device activated and reached the 3-month postactivation test interval. At the 6-month interval, 49 subjects (98%) completed all effectiveness outcome assessments, while 48 completed the audiometric testing for hearing sensitivity. One subject's data were not obtained since this subject was explanted and reimplanted with a Nucleus 5 cochlear implant between the 3- and 6-month intervals due to profound loss of low-frequency hearing and poor performance at 3-months post-activation. An additional subject completed effectiveness outcome assessments, but did not complete the audiometric testing at the 6-month interval. Of the 49 subjects available at the 12-month interval, 46 subjects were assessed, while three subjects were not evaluated. One subject was explanted and reimplanted with a Nucleus Freedom™ cochlear implant prior to the 12-month interval. The remaining two subjects withdrew prior to reaching the 12-month interval: one subsequent to a diagnosis of pancreatic cancer, and the other due to advancing dementia.

C. Study Population Demographics and Baseline Parameters

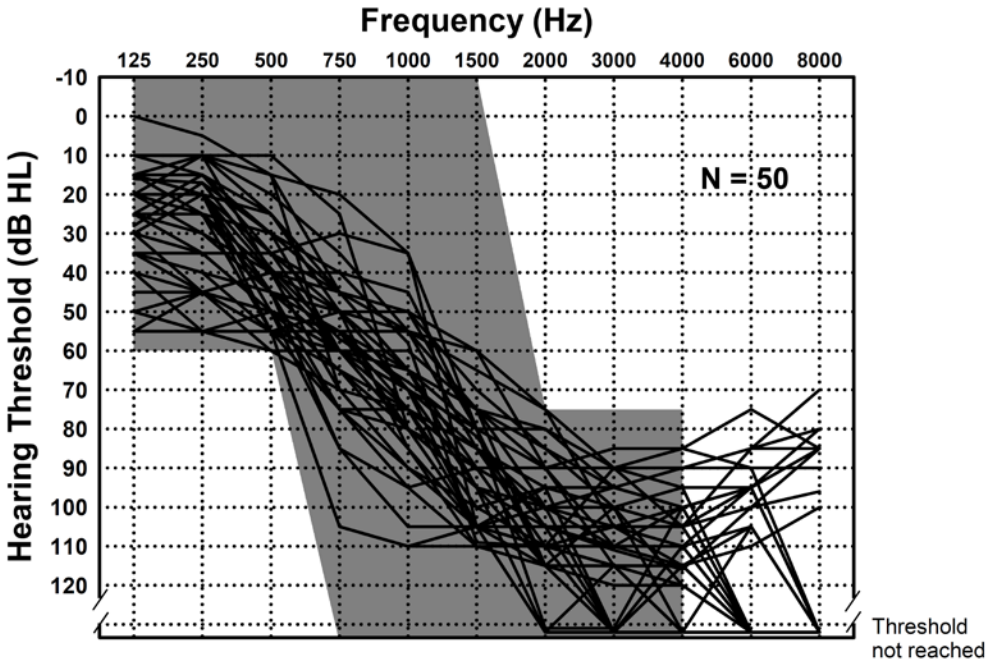
Of the 50 implanted subjects, 25 were female. At the time of implantation, subjects ranged in age from 23 to 86.2 years. The duration of hearing loss (of any degree) ranged from 6 to 84 years. The duration of severe to profound high-frequency hearing loss ranged from 1.6 to 30.1 years. Other subject demographics are summarized in Table 9 below.

Table 9. Descriptive statistics for subject variables

Variable	*Mean*	*SD*	*Min*	*Max*
Age at implantation (years)	64.1	14.7	23.0	86.2
Duration of hearing loss of any degree (years)	28.1	14.9	3.4	73.9
Duration of severe-to-profound high-frequency hearing loss (years)	13.1	7.2	1.6	30.1
Preoperative CNC word score (%)	28.4	14.7	9	64
Preoperative low-frequency hearing sensitivity (from 125-1000 Hz, dB HL)	45.3	10.2	19	63

Figure 2 below shows the preoperative unaided air conduction thresholds in the ear to-be-implanted for all subjects. The shaded region represents the range of audiometric thresholds according to the subject candidacy criteria. Consistent with the study inclusion criteria, hearing thresholds ranged from within normal limits to moderately severe loss up to 500 Hz, sloping downward to severe or profound loss at higher frequencies.

Figure 2. Individual subjects' pre-operative audiograms (curves), audiometric fitting range (gray region).



D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on all 50 implanted patients. The key safety outcomes for this study are presented below in Table 10 through Table 12.

Adverse effects that occurred in the PMA clinical study:

Many of the 10 possible anticipated adverse events (defined earlier) were reported by the applicant to have occurred during the study. In summary, a total of 71 adverse events were reported (see Table 10 below). Of the 50 implanted subjects, 34 (68%) experienced at least one adverse event. Multiple (2-4) adverse events were experienced by 20 of 50 subjects. 24 of 71 adverse events in 23 subjects were unresolved during the study.

Table 10. Number and percentage of adverse events observed for Hybrid L24 subjects.

Event	Number of Events	Percent of Events	Number of Subjects with Event	Percent of Subjects	Percent Resolved
Profound/Total loss of hearing[1]	22	31.0%	22	44.0%	0.0%
Open/short circuited electrodes[2]	11	15.5%	11	22.0%	100.0%
Increased tinnitus	6	8.5%	6	12.0%	100.0%
Tinnitus not present preoperatively	6	8.5%	6	12.0%	100.0%
Explantation/ Reimplantation	6	8.5%	6	12.0%	100.0%
Dizziness	3	4.2%	3	6.0%	100.0%
Dizziness with change in hearing	2	2.8%	2	4.0%	100.0%
Increased tinnitus with change in hearing	2	2.8%	2	4.0%	100.0%
Skin irritation due to externals	2	2.8%	2	4.0%	100.0%
Sound quality issue	2	2.8%	2	4.0%	50.0%
Decrease in performance[3]	1	1.4%	1	2.0%	0.0%
Imbalance	1	1.4%	1	2.0%	100.0%
Imbalance with change in hearing	1	1.4%	1	2.0%	100.0%
Increased impedances with change in hearing	1	1.4%	1	2.0%	100.0%
Local stitch infection	1	1.4%	1	2.0%	100.0%
Overstimulation[2]	1	1.4%	1	2.0%	100.0%

Event	Number of Events	Percent of Events	Number of Subjects with Event	Percent of Subjects	Percent Resolved
Pain in implant ear	1	1.4%	1	2.0%	100.0%
Vertiginous symptoms with change in hearing	1	1.4%	1	2.0%	100.0%
Vertigo	1	1.4%	1	2.0%	100.0%
Total	**71**				

Notes: [1]Although "Sudden changes in residual low-frequency hearing" or "Total loss of residual hearing" were specified in the applicant's protocol, profound/total loss was used as the actual criteria for reporting by applicant. Smaller amounts of hearing loss are discussed below. [2]In terms of the list of adverse effects defined in section VIII, open/short circuited electrodes and overstimulation both fall under device-related/programming problems. [3]Subject explanted/reimplanted with traditional CI on August 26, 2013.

As listed in Table 10, the two most frequently observed adverse events, reported as resolved, were tinnitus-related issues and device-related open shorts experienced by 28% and 22% of subjects, respectively.

In terms of the unresolved adverse events observed in this study, profound/total loss of residual low-frequency hearing was by far the most frequently observed adverse event, occurring in 22 of 50 (44%) of subjects. Six of these subjects were subsequently explanted and reimplanted with a traditional cochlear implant. Loss of residual hearing and device explants are discussed further below.

Loss of residual low-frequency hearing

The proportions of subjects stratified by the amount of low-frequency hearing loss at the 6- and 12-month intervals are summarized in Table 11. The same data, stratified by postoperative residual low-frequency hearing sensitivity, are summarized in Table 12.

Table 11. Proportion of subjects with various amounts of low-frequency hearing loss at 6 and 12 months

Amount of loss in low-frequency hearing (dB)	*6-month (N = 50[1])*	*12-month (N = 46[2])*
≤ 10	24.0% (12/50)	19.9% (9/46)
≤ 20	48.0% (24/50)	45.7% (21/46)
≤ 30	54.0% (27/50)	58.7% (27/46)
> 30	46.0% (23/50)	41.3% (19/46)

[1]Based on the data imputed using LOCF for two subjects with missing data at 6 months.
[2]Based on the data obtained from all subjects evaluated at 12 months.

Table 12. Proportion of subjects' low-frequency hearing sensitivity at 6 and 12 months

Residual low-frequency hearing sensitivity (dB HL)	*6-month (N = 50)*	*12-month (N = 46)*
41 – 55 (Moderate loss)	30.0% (15/50)	32.6% (15/46)
56 – 70 (Moderately severe loss)	18.0% (9/50)	21.7% (10/46)
71 – 90 (Severe loss)	18.0% (9/50)	17.4% (8/46)
> 90 & measurable (Profound)	24.0% (12/50)	17.4% (8/46)
no measurable hearing (Total/Profound loss)	10.0% (5/50)	10.9% (5/46)

As shown across Table 10 and Table 12, profound/total loss of residual low-frequency hearing was experienced by 22 of 50 (44%) of subjects for whom data were available at the time of the PMA submission (i.e., May 30, 2013). Regarding the time course of these losses, 17 subjects experienced the loss by six months post implantation and the remaining five experienced the loss later: one subject by 12 months, two by 18 months, one by 36 months, and one by 48 months. Regarding the amount of loss in their residual low-frequency hearing as of May 30, 2013, 30 of 50 subjects (60%) exhibited more than a 30 dB loss. Five of these subjects' hearing sensitivity later exhibited a loss within 30 dB of preoperative levels as revealed at their most recent follow-up session.

Device Explants

At the time of this PMA submission, 4 subjects were reported to have been explanted and reimplanted. Of the 4 subjects, one subject was explanted and re-implanted between 3 and 6 months post activation, a second subject between 6 and 12 months, and the remaining two subjects after 12 months. The reported reasons for explantation and reimplantation in the first subject included partial electrode shorts, loss of hearing, and poor performance. The three other subjects sought explantation and reimplantation due to hearing loss, poor performance, and dissatisfaction with regards to device outcomes. All four subjects were reimplanted with traditional cochlear implants: one subject was implanted with the CI512 and the other three with the CI24RE. Available preliminary data suggest that performance of these 4 reimplanted subjects is no worse than pre-revision.

On October 24, 2013, the applicant reported that two additional subjects had undergone explantation/reimplantation, both at the end of August 2013. One of these two subjects was initially reported as having profound hearing loss at initial activation and unresolved decreased performance, as discussed earlier. The other subject had improved performance up until 12 months. Following the 12 month period, this subject withdrew from the study; only limited data regarding this subject's pre and post explant performance were provided.

Table 13 summarizes baseline characteristics of the six explanted subjects including age, gender, duration of hearing loss prior to implantation, and pre-

operative low-frequency hearing threshold average. Based on this small sample of explanted subjects, none of these baseline characteristics is observed to be a predictor of the need for explantation/reimplantation.

Table 13. Baseline characteristics of explanted subjects

Age (years)	Gender	Duration of loss prior to implantation (Years)	Etiology of hearing loss	Pre-op low-frequency threshold (dB HL)	Explant/Re-Implant reason
67	Female	42	Unknown etiology	60	Residual hearing loss, partial shorts, poor performance
71	Male	41	Noise exposure	44	Residual hearing loss, dissatisfied
66	Male	15	Ototoxic drugs	43	Residual hearing loss, dissatisfied
81	Female	74	Familial	49	Residual hearing loss, dissatisfied
68	Male	13	Unknown etiology	47	Residual hearing loss
78	Male	38	Unknown etiology	51	Residual hearing loss, decreased performance

Sound quality issues and decreased performance

As shown in Table 10, sound quality issues and decrease performance were reported as unresolved adverse events. Of the two subjects who experienced sound quality issues, in one subject, the event remained unresolved during the study. This subject reported a “static sound” in the presence of speech, at the device programming follow up approximately a month after implantation. Although no receiver/stimulator malfunction was reported per integrity testing

and despite the use of new sound processors and multiple programming sessions, the static sound persisted.

One subject was reported as having experienced decreased hearing performance. This subject had profound loss of residual hearing at initial activation and an additional decrease in electrical hearing performance following the 3-month interval. On October 24, 2013, the applicant reported that this subject has been explanted and re-implanted with a traditional cochlear implant.

2. Effectiveness Results

The analysis of effectiveness was based on the previously defined co-primary and secondary effectiveness endpoints at the 6-month time point. Key effectiveness outcomes are presented in Table 14 through Table 23. Also included below are definitions of the test methods.

Co-Primary Effectiveness Endpoints

As summarized in Table 14, statistically significant improvements in mean CNC word score and mean AzBio sentence-in-noise score occurred from the (Acoustic Alone, hearing-aided) baseline to the 6-month interval postactivation (Hybrid condition). As stated earlier, both measures were conducted on the ipsilateral ear only. Hence, both co-primary effectiveness endpoints were met. These data are based on 49 of 50 (98%) subjects who were assessed at the 6-month interval. When worst-case imputed scores for the missing subject were included in the sample, both co-primary endpoints were still met: the mean improvement with 95% confidence intervals was 35.7% (27.8%, 43.6%) for CNC words and 32.0% (23.6%, 40.4%) for AzBio. These analyses revealed that the results for co-primary endpoints are robust to the missing data.

Table 14. Co-primary effectiveness endpoints results

	Baseline **Mean ± SD (%)**	**6 Month** **Mean ± SD (%)**	**Change** **Mean ± SD (%)**	**95% CI (%)**	***p*-value**
CNC Words	28.4 ± 14.9	65.4 ± 25.4	37.0 ± 26.6	(29.4, 44.6)	< 0.0001
AzBio Sentences in Noise	16.4 ± 14.5	49.2 ± 30.8	32.8 ± 29.1	(24.5, 41.2)	< 0.0001

Secondary Effectiveness Endpoints

Table 15 displays the proportion of subjects who performed poorer, similar, and better in the Hybrid condition for each of the three secondary endpoint metrics at the 6-month interval, when compared to the ipsilateral Acoustic Alone baseline condition. Since over 75% of the subjects exhibited similar or better performance on all three metrics, it was concluded that all secondary endpoints were met. Of note, however, there were small proportions of subjects who performed poorer for CNC word accuracy (4.0%), CNC phoneme accuracy (10.0%), and AzBio score (12.0%), respectively, at the 6-month interval compared to preoperative baseline.

Table 15: Proportion of subjects who performed poorer, similar, or better in the Hybrid versus the (ipsilateral) Acoustic Alone condition at 6 months

Endpoint	*Poorer*	*Similar*	*Better*
CNC Words	4.0% (2/50)	16.0% (8/50)	80.0% (40/50)
CNC Phonemes	10.0% (5/50)	6.0% (3/50)	84.0% (42/50)
AzBio Sentences	12.0% (6/50)	16.0% (8/50)	72.0% (36/50)

Although not prospectively defined in their protocol, the applicant and the FDA also analyzed the secondary endpoints in the bilateral "Everyday Listening" condition (defined under "*Test Conditions"* in Section X.A.3 above) at 6 months and compared with the preoperative Bilateral Acoustic condition (i.e., with two hearing aids). Table 16 displays the proportion of subjects' scoring poorer, similar, or better at 6 months as compared to preoperative baseline. All subjects' scores were similar or better for all three secondary endpoints.

Table 16: Proportion of subjects who performed poorer, similar, or better in the Everyday Listening versus the Bilateral Acoustic condition at 6 months for each secondary endpoint

Endpoint	*Poorer*	*Similar*	*Better*
CNC Words	0% (0/50)	12.0% (6/50)	88.0% (44/50)
CNC Phonemes	0% (0/50)	10.0% (5/50)	90% (45/50)
AzBio Sentences	0% (0/50)	16.0% (8/50)	84% (42/50)

The increase in the proportion of subjects performing similar to or better than baseline in the Everyday Listening (bilateral) versus the Hybrid (unilateral) conditions highlights the importance of the contribution of the residual low-frequency hearing in the non-implanted ear. These results support the unilateral intended use for the Hybrid L24.

3. Subgroup Analyses

Exploration of Effects of Baseline Characteristics on Device Effectiveness

To explore the influence of baseline characteristics on effectiveness outcomes, post hoc simple regression and multivariate analyses were conducted. Simple regression analysis was conducted to assess the effects of baseline characteristics on the co-primary endpoints. For this analysis, each of the two co-primary effectiveness endpoint variables (improvements in CNC Words and AzBio Sentences in Noise) was regressed on each of the six baseline covariates: gender, age at implantation, duration of hearing loss, duration of severe to profound high-frequency hearing loss, baseline CNC word scores, and pre-operative hearing threshold. Multivariate regression analyses were further performed as many of the baseline covariates were correlated. More specifically, three baseline covariates, age at implantation, duration of hearing loss, and gender were correlated. Further, age at implantation and duration and hearing loss were positively correlated.

The six baseline variables (gender, in addition to the five listed in Table 9) were included in the multivariate regression model for all 50 subjects. Among the six covariates, two baseline variables, i.e., duration of hearing loss and pre-operative low-frequency hearing thresholds were observed to be negatively associated with both co-primary endpoints (CNC and AzBio). Table 17 displays the results from this multivariate regression analysis. These results suggest that a shorter duration of hearing loss and/or better pre-operative low-frequency hearing sensitivity may be associated with better effectiveness outcomes.

Table 17. Results from multivariate regression analysis for each co-primary effectiveness endpoint on all six baseline subject characteristics

Subject characteristic	*Improvement in CNC scores*		*Improvement in AzBio scores*	
	Estimate	*p-value*	*Estimate*	*p-value*
Gender (female vs. male)	8.98	0.194	9.05	0.259
Age at implantation (years)	-0.39	0.134	-0.31	0.303
Duration of hearing loss (years)	-0.54	**0.039**	-0.63	**0.038**
Duration of severe hearing loss (years)	0.22	0.634	0.45	0.413
CNC Words (%)	-0.85	**0.001**	-0.34	0.246
Low-frequency hearing threshold (dB HL)	-0.84	**0.023**	-1.08	**0.013**

Device Effectiveness as a Function of Loss of Low-Frequency Hearing

Various post hoc analyses were conducted to examine device effectiveness as a function of subjects' loss of residual low-frequency hearing. In these analyses, all missing 6-month data were imputed with the corresponding 3-month data.

Hearing loss treated as a continuous variable: Simple regression analysis revealed a negative correlation between each co-primary endpoint (improvement in CNC words and improvement AzBio sentences in noise) and loss of residual low-frequency hearing. Loss of low-frequency hearing was analyzed in two ways: by the amount of change of low-frequency thresholds and by the (final) low-frequency hearing sensitivity threshold at 6 months. It was observed that the more low-frequency hearing was preserved, the better the device effectiveness.

Hearing loss treated as a discrete variable: The consistency of the co-primary endpoints based on individual subjects' was further examined post hoc by the residual low-frequency hearing preserved at the 6-month interval. In the analysis presented here, the low-frequency hearing sensitivity at the 6-month interval was divided into the following four ranges: 41 through 55 dB HL (a moderate loss), 56 through 70 dB HL (a moderate-severe loss), 71 through 90 dB HL (a severe loss), and poorer than 90 dB HL (a profound and possibly also total loss). The results are displayed in Table 18 and Table 19.

Table 18: Proportion of subjects who performed poorer, similar, or better for CNC Word Recognition in Hybrid versus Acoustic Alone condition, as a function of residual low-frequency hearing sensitivity at 6 months

Low-frequency hearing sensitivity (dB HL)	*Mean (STD) (%)*	*Proportion of subjects*			
		Poorer	*Similar*	*Better*	*Total*
> 40, ≤ 55	47.3 (22.6)	0% (0/50)	**2% (1/50)**	26% (13/50)	28% (14/50)
> 55, ≤ 70	48.9 (19.2)	0% (0/50)	0% (0/50)	20% (10/50)	20% (10/50)
> 70, ≤ 90	44.1 (19.2)	0% (0/50)	0% (0/50)	18% (9/50)	18% (9/50)
> 90	14.2 (28.0)	**4% (2/50)**	**14% (7/50**)	16% (8/50)	34% (17/50)

Table 19. Proportion of subjects who performed poorer, similar, or better for AzBio Sentence-in-Noise Test in Hybrid versus Acoustic Alone condition, as a function of residual low-frequency hearing sensitivity at 6 months

Low-frequency hearing sensitivity (dB HL)	*Mean (STD) (%)*	*Proportion of subjects*			
		Poorer	*Similar*	*Better*	*Total*
> 40, ≤ 55	45.0 (22.1)	0% (0/50)	**2% (1/50)**	26% (13/50)	28% (14/50)
> 55, ≤ 70	47.5 (25.2)	0% (0/50)	0% (0/50)	20% (10/50)	20% (10/50)
> 70, ≤ 90	41.9 (27.9)	0% (0/50)	**2% (1/50)**	16% (8/50)	18% (9/50)
> 90	7.0 (22.0)	**12% (6/50)**	**12% (6/50)**	10% (5/50)	34% (17/50)

Among those subjects with residual low-frequency hearing sensitivity poorer than 90 dB HL (N = 17), 47.1% (N = 8) performed either similarly or poorer (i.e., did not improve) in both the CNC Word Recognition Test and the AzBio Sentence-in-Noise Test (Table 20).

Table 20: For subjects with residual low-frequency hearing sensitivity thresholds poorer than 90 dB HL, proportions with poorer, similar, or better for CNC Word Recognition scores and AzBio Sentence-in-Noise scores in the Hybrid condition

AzBio / *CNC*	*Poorer*	*Similar*	*Better*	*Total*
Poorer	**11.8% (2/17)**	0% (0/17)	0% (0/17)	11.8% (2/17)
Similar	**17.7% (3/17)**	**17.7% (3/17)**	5.9% (1/17)	41.2% (7/17)
Better	5.9% (1/17)	17.7% (3/17)	23.5% (4/17)	47.1% (8/17)
Total	35.3% (6/17)	35.3% (6/17)	29.4% (5/17)	100% (17/17)

To further investigate the relationship of hearing loss with device effectiveness and evaluate benefit-risk, the applicant conducted post hoc analysis by classifying hearing sensitivity at 6 months into two groups. Group 1 consisted of subjects

whose low-frequency hearing thresholds were better than or equal to 90 dB HL and Group 2 consisted of subjects whose low-frequency hearing thresholds were poorer than 90 dB HL (i.e., profound/total loss of residual low-frequency hearing).

In terms of CNC word recognition scores, the mean of Group 1 is 47% (SD = 20%), which is remarkably higher than the mean of Group 2: 14% (SD = 28%). This suggests that preservation of residual hearing is important for CNC word recognition. Table 21 lists the counts and proportions of subjects whose 6-month scores were poorer than, similar to, or better than the pre-op scores by group. It can be observed that, in Group 1, almost all subjects improved in CNC word recognition performance, whereas, in Group 2, only about half of the subjects did.

Table 21. Improvement in CNC words: Group 1 versus Group 2

	Poorer	**Similar**	**Better**
Group 1 (≤ 90 dB HL)	0/33 (0%)	1/33 (3%)	32/33 (97%)
Group 2 (> 90 dB HL)	2/17 (12%)	7/17 (41%)	8/17 (47%)

The mean AzBio score of Group 1 is 45% (SD = 24%) which is remarkably higher than the corresponding score for Group 2: 7% (SD = 22%). This suggests that preservation of residual hearing is important for AzBio sentence test. Table 22 lists the counts and proportions of subjects whose 6-month AzBio score were poorer than, similar to, or better than the pre-op scores by groups. In Group 1, almost all subjects improved the AzBio test scores, whereas, in Group 2, only about a third of the subjects improved, while a third of subjects performed poorer.

Table 22. Improvement in AzBio sentences: Group 1 versus Group 2

	Poorer	**Similar**	**Better**
Group 1 (≤ 90 dB HL)	0/33 (0%)	2/33 (6%)	31/33 (94%)
Group 2 (> 90 dB HL)	6/17 (35%)	6/17 (35%)	5/17 (30%)

To help characterize device effectiveness in terms of benefit, FDA defined benefit post hoc as improvement on at least one co-primary endpoint test. These data are summarized in Table 23 as proportions out of all 50 subjects.

Table 23. Device Benefit vs. Residual Hearing Preservation (6 mo)

	Benefit	Proportion
Group 1 (≤ 90 dB HL)	Yes	33/50 (66%)
Group 2 (> 90 dB HL)	Yes	9/50 (18%)
	No	8/50 (16%)

For Group 1 subjects, all 33 subjects improved in at least one test. However, for Group 2 subjects, 8 of 17 did not improve in either test: two were poorer in both AzBio and CNC, three were poorer in AzBio with no change in CNC, and three had similar AzBio and CNC scores.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 10 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The applicant included test results on the following additional tests in their PMA: SRT in Noise, UW-CAMP, SSQ, DUQ, and MBQ. Results from these tests are briefly summarized below.

Speech Recognition Threshold (SRT) in Noise Test – Significant improvements from the preoperative measurements were reported. Specifically, adding ipsilateral acoustic hearing offered an average of 1.2 dB over contralateral acoustic hearing alone. Bilateral acoustic hearing offered an average SRT advantage of 1.6 dB over contralateral ear alone. Notably, not all subjects completed each test at the 6-month interval: data for this test were only collected from 35 subjects, of whom 30 had some amounts of preserved low-frequency hearing in the implanted ear. In other words, any improvement reported was largely limited to only those subjects with some amounts of residual low-frequency following implantation. The fact that the applicant did not obtain data for the remaining 15 subjects with little or no residual low-frequency hearing makes it difficult to draw any conclusion based on the data set.

The University of Washington Clinical Assessment of Music Perception (UW-CAMP) – The UW-CAMP (Nimmons et al., 2008), a music perception test battery psychometrically validated in adult cochlear implant recipients (Kang, 2009), was adopted to assess subjects' music perception abilities. The UW-CAMP consists of three subtests: pitch discrimination (measured in semitones), melody recognition and perception of timbre (measured in percent correct). The UW-CAMP was administered ipsilaterally and bilaterally at the preoperative baseline and at 6 months. The mean, standard deviation, and number who completed the test are presented in Table 24 for each subtest. The data across all subtests indicate no significant changes between the performance at preoperative baseline and at 6 months for each subset, for both the unilateral and also the bilateral comparisons.

Table 24: Descriptive statistics (Mean ± Standard Deviation)) for UW-CAMP subtests: pitch discrimination, melody and timber identification

Subtest	*Ipsilateral (implanted ear alone)*		*Bilateral (both ears)*	
	Acoustic at baseline	*Hybrid at 6 months*	*Bilateral at baseline*	*Everyday Listening at 6 months*
Pitch (semitone)	1.1 ± 1.0 (N = 50)	1.4 ± 1.5 (N = 46)	1.1 ± 1.1 (N = 50)	1.0 ± 0.8 (N = 46)
Melody (% correct)	66.2 ± 25.7 (N = 50)	65.9 ± 29.5 (N = 47)	66.3 ± 24.8 (N = 47)	66.7 ± 25.0 (N = 46)
Timbre (% correct)	50.8 ± 18.2 (N = 50)	56.6 ± 22.7 (N = 47)	56.2 ± 19.8 (N = 47)	57.0 ± 19.6 (N = 46)

Changes in UW-CAMP subtest scores were also analyzed for the ipsilateral ear only by the two previously defined subgroups: Group 1 (thresholds better than 90 dB HL) and Group 2 (thresholds poorer than or equal to 90 dB HL). The purpose of these additional analyses conducted by FDA was to explore the effects of residual hearing on music perception subtests since acoustical low-frequency hearing is considered important for music perception. Table 25 summarizes the results. Group 2 on average performed more poorly at 6 months compared to baseline in two subtests: pitch discrimination and melody identification. Group 1, by contrast, on average improved in all three subtests, and to a greater extent in timbre recognition than Group 2.

Table 25. Change in UW-CAMP subtest scores (6-month score minus baseline score) for the ipsilateral ear, by subgroup

	Group 1 Change Mean (SD)	Group 2 Change Mean (SD)	Change Difference (Group 1 – Group 2)
Pitch (semitone)	-0.13 (0.92) N=32	1.32 (2.20) N=14	-1.45
Melody (%)	1.7 (10.41) N=32	-10.0 (19.5) N=15	11.7
Timbre (%)	6.8 (19.3) N=32	1.3 (19.2) N=15	5.5

Speech, Spatial, and Qualities of Sound Questionnaire (SSQ) – SSQ includes three hearing domains: (1) hearing for speech in quiet and noisy conditions, (2) spatial hearing, and (3) sound quality. Fifty subjects completed the SSQ preoperatively and 48 completed it at 6 months. Higher scores indicate positive responses. For each subject, the average scores were computed for each hearing domain. Scores for the three subscales were averaged to derive a total score. The comparisons were made between the preoperative baseline and 6-month postoperative time point, as shown in Table 26. The results indicate that the SSQ scores improved at 6 month postoperatively from the preoperative baseline.

Table 26: Descriptive statistics (N, mean, standard deviation) of SSQ at pre-operative baseline and 6-month time point

Subscale	*Pre-operatively*			*6 months*		
	N	*mean*	*std*	*N*	*mean*	*std*
Speech/Hearing	50	3.2	1.3	48	5.4	1.7
Spatial	50	4.5	1.9	48	5.5	1.7
Quality	50	5.0	1.5	48	6.3	1.4
Total	50	4.2	1.3	48	5.7	1.3

Device Use Questionnaire (DUQ) – A total of 48 subjects completed the DUQ at 6 months. The result indicates that, in terms of the preferred way of listening, 65% (34/48) preferred the Combined mode, 29% (14/48) preferred the Bimodal mode, while 6% (3/48) preferred the Hybrid mode. Regarding the "overall satisfaction with their performance with the Hybrid L24 Implant System," 79% (38/48) reported being very satisfied or satisfied, 6% (3/48) reported being neutral, while 15% (7/48) reported being dissatisfied or very dissatisfied. A total of 15 subjects with profound loss of hearing completed the DUQ. Regarding satisfaction "with their performance using their preferred way of listening", among these 15 subjects, 80% (12) reported being very dissatisfied or

dissatisfied, 7% (1/15) reported being neutral, while 13% (2/15) reported being satisfied or very satisfied.

Musical Background Questionnaire (MBQ) – This questionnaire was adopted to examine musical training prior to hearing loss, listening habits, satisfaction with music listening, quality of music, enjoyment of musical styles, enjoyment of different instrumental timbres. This questionnaire was completed by preoperatively (N = 50) and at the 6-month interval (N = 48). The results provided by the applicant address certain aspects of the MBQ considered as the key aspects. For example, subjects reported an increase in musical enjoyment and an increase in the number of hours of music listening after receiving a Hybrid L24. Similarly, at the 6-month interval, 83.4% (40/48) of the subjects reported preferring to listen to music in the Combined Mode or Bimodal Mode. Together, the results from MBQ do not reveal any evidence that music enjoyment is compromised when music listening was achieved when bilateral (electric and acoustic) inputs were available.

Together, the patient-reported outcomes as derived from the SSQ, DUQ, and MBQ indicate overall improvement or no change in perceived benefits and satisfaction with the Hybrid L24 post-operatively than pre-operatively. There are, however, some inherent limitations with the SSQ, DUQ, and MBQ findings in the context of this study. First, not all of these instruments were psychometrically validated for the intended patient population for the Nucleus Hybrid L24. Second, because the present study design lacks a control group and is not blinded, interpretation of the questionnaire results may be biased by the placebo effect.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

A. Panel Meeting Recommendation

At an advisory meeting held on November 8, 2013 the Ear, Nose, and Throat Devices Panel . voted 14-0-0 (yes-no-abstain) that there is reasonable assurance that the device is safe, 14-0-0 that there is reasonable assurance that the device is effective, and 13-0-1 that the benefits of the device outweigh the risks in patients who meet the criteria specified in the proposed indication.

The 24-hour panel-meeting summary is available at the following link: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/EarNoseandThroatDevicesPanel/ucm373789.htm

B. FDA's Post-Panel Action

FDA accepts the Panel's recommendations. Given the available data and the Panel discussion concerning the indicated population, FDA subsequently recommended that the device be indicated for unilateral use at this time, and the applicant agreed.

Additional clarifications to the device labeling including the indications for use have also been made based on Panel discussion and the clinical study.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Two co-primary and three secondary effectiveness endpoints were defined. For all endpoints, performance at six months post implantation was compared to pre-operative baseline. Performance was primarily measured unilaterally, i.e., using the Hybrid L24 alone (at 6 months) and compared to the preoperative, hearing aided performance in the ear-to-be-implanted (at preoperative baseline). The two co-primary effectiveness endpoints were defined as a mean improvement in CNC word and AzBio sentence-in-noise scores. Three secondary effectiveness endpoints were defined in terms of the proportion of subjects who performed similar to or better at 6 months versus baseline for the following metrics: CNC words, CNC phonemes, and AzBio sentences in noise.

Co-Primary Endpoint Results: The mean improvement in CNC words was 35.7% with 95% confidence intervals of (27.8%, 43.6%). The mean improvement in AzBio was 32.0% with 95% confidence intervals of (23.6%, 40.4%). These improvements were statistically significant (both *p*-values < .0001), and it was thus concluded that both co-primary endpoints were met.

Secondary Endpoint Results: More than 75% of the subjects performed similar to or better on each of the three specified measures: CNC words (96%), CNC phonemes (90%), and AzBio (88%). All secondary endpoints were met.

Other effectiveness measures and analyses

Everyday Listening (Bimodal and Combined) testing: Data were also collected bilaterally (i.e., including a hearing aid on the contralateral side at 6 months) and compared with the baseline bilaterally aided condition. For each of the three secondary endpoints, all of subjects' scores (100%) were similar to or better than their preoperative performance.

Effect of baseline characteristics on endpoints: Post hoc analysis was conducted to see which, if any, of the six baseline variables (age, gender, duration of hearing loss of any degree, duration of severe-to-profound high-frequency hearing loss, preoperative CNC word score, or preoperative low-frequency hearing sensitivity) affected outcome(s). Multivariate analyses revealed that two baseline characteristics (pre-operative low-frequency hearing thresholds and duration of hearing loss) were each negatively associated with both CNC words and AzBio. The inference from these results is that a better pre-operative low-frequency hearing threshold and/or a shorter duration of hearing loss may be associated with better effectiveness performance.

Effect of postoperative low-frequency residual hearing on effectiveness: Post hoc analyses were conducted to examine the effect of postoperative low-frequency hearing on effectiveness. The common finding from these analyses was that the more hearing that was preserved, the better the outcome. This occurred when residual hearing sensitivity, or alternatively, the amount of hearing loss, was treated as either a continuous or a discretized variable (due to stratification).

When hearing loss was treated as a continuous variable, there was a negative correlation between each of the co-primary endpoints and loss of residual low-frequency hearing, both in terms of the amount of the amount of low-frequency loss and the hearing sensitivity (i.e., hearing thresholds) at 6 months. That is, the more preserved low-frequency hearing at 6 months, the better the device effectiveness.

In terms of analysis by discretized levels of hearing loss, the applicant stratified postoperative low-frequency hearing sensitivity into two groups: Group 1 (thresholds better than 90 dB HL) or Group 2 (thresholds poorer than or equal to 90 dB HL). Of the 50 subjects, 33 (66%) were thus classified as Group 1 and 17 (34%) as Group 2. In terms of CNC word recognition scores, the mean of Group 1 was 47% (SD = 20%), which greatly exceeded the mean of Group 2: 14% (SD = 28%). This suggests that preservation of residual hearing is important for CNC word recognition. In addition, almost all Group 1 subjects improved in CNC word recognition performance, whereas, in Group 2, only about half of the subjects did. The mean AzBio score of Group 1 was 45% (SD = 24%) while for Group 2 was 7% (SD = 22%) suggesting that preservation of residual hearing is important for AzBio sentence recognition. In addition, almost all Group 1 subjects improved their AzBio test scores from baseline, whereas, in Group 2, only about a third of the subjects improved, while a third of subjects performed more poorly.

Benefit was defined post hoc by FDA as improvement on at least one co-primary endpoint test at 6 months versus baseline. For Group 1 subjects, all (100%) of the 33 subjects improved in at least one test. However, for Group 2 subjects, nearly half (8/17) did not improve in either test.

Analysis by study site: The consistency of the primary endpoints was examined across investigational sites by testing for an effect of site in an ANOVA model, based on 49 subjects who completed the 6-month speech recognition tests. The results indicated no evidence of site effects on the primary effectiveness endpoints.

Other Effectiveness Measures:

UW-CAMP Music Perception: The results from 46 subjects with available data at 6 months postactivation indicated no change in performance on each of the three subtests compared to baseline. Further analysis revealed that subjects who experienced profound/total loss of residual low-frequency hearing performed, on average, more poorly compared to baseline on two UW-CAMP subtests: pitch discrimination and melody identification.

B. Safety Conclusions

The risks of the device are based on the data collected in the clinical study conducted to support PMA approval as described above.

The primary safety objective was to report all surgical and/or device-related events, as the number and proportion of individuals experiencing an adverse event.

- Loss of residual low-frequency hearing was the most frequently observed anticipated unresolved adverse event. Profound/Total loss was observed in 22 of 50 subjects (44%).
- Tinnitus related issues, device related open shorts, and dizziness related issues were the most frequently observed resolved adverse events and occurring at a rate of 28, 22, and 18%, respectively, in the 50 enrolled and implanted subjects.
- Explantation and reimplantation with a standard cochlear implant occurred in 6/50 (12%) of subjects as of February 10, 2014.

Observed adverse events that were resolved were consistent with those seen with approved cochlear implant systems. It is yet to be determined over the long-term how many additional subjects who experience profound loss will be explanted and re-implanted with a traditional cochlear implant array. The post approval studies which are specified in the approval order are designed to assess the time course of hearing loss and explant/reimplant rate. Based on the results of these post approval studies, the labeling for the Hybrid L24 will be updated accordingly.

C. Benefit-Risk Conclusions

There are limited options for the indicated population as reflected in the poor CNC word recognition performance even with appropriately fit bilateral hearing aids. The clinical study results for the Hybrid L24 that, on average, the Hybrid L24 is expected to improve speech recognition (in terms of CNC words and AzBio sentences) for a majority of the indicated population.

However, the profound and possibly also total loss of low-frequency hearing that occurred in 22/50 (44%) of subjects is a known risk and renders the device usage to electrical (cochlear implant) stimulation only since the acoustic amplification is ineffective for these levels of hearing loss. For subjects who lost low-frequency residual hearing to the profound/total level(s), the device showed benefit for only about half (9 of 17) or 53% of these subjects. Furthermore, 6/50 subjects who lost residual low-frequency hearing chose to undergo explantation of the Hybrid L24 and be reimplanted with an approved standard cochlear implant. The long-term rate of explantation/reimplantation is being studied in a post-approval study.

The clinical study results highlight the importance of preserving residual hearing in the contralateral ear since all subjects performed similar to or better than baseline in the Everyday Listening conditions (which utilize acoustic hearing in the contralateral, non-implanted ear) versus the Hybrid (alone) condition. These results indicate the important role of contralateral acoustic hearing for device effectiveness and support the indication for unilateral use for the device at this time.

FDA has determined that the overall hearing benefits of the device outweigh this risk for this population who do not benefit from traditional hearing aids. Prospective patients should carefully discuss all benefits and risks of this new device with their physicians. In terms of fitting the device and patient counseling, clinicians should consider the duration of hearing loss for potential candidates since this is listed in both in the contraindications (device labeling) and in the exclusion criteria for the clinical study. This advisory is also supported by the exploratory analysis suggesting that a shorter duration of hearing loss and/or better pre-operative low-frequency hearing sensitivity may be associated with better effectiveness performance.

Given the benefit-risk profile for the device, the Indications for Use for the Hybrid L24 clearly lists the following restrictions: unilateral usage of the device and a sufficient trial of conventional hearing aids. The labeling also includes a sufficiently detailed and complete summary of the study finding for clinicians and provides counseling recommendations based on the clinical study results.

These recommendations were discussed during the November 8, 2013 panel meeting for the Hybrid L24 where the Panel voted 13-0-1 (yes, no, abstain) that the benefits of the Hybrid L24 do outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

D. Overall Conclusions

The data in this application support a reasonable assurance of safety and effectiveness of this device when used in accordance with the proposed indications for use. The provided preclinical testing for the device was acceptable. Based on the clinical study results, it is reasonable to expect clinical benefits with use of the Nucleus Hybrid L24 Cochlear Implant System in terms of improvement in speech understanding in quiet and noise since the average performance of the study population showed statistically significant improvements in these two co-primary endpoint measures. While improvement was observed on the average, for individuals who lost residual low-frequency hearing to the profound level, the device was less likely to provide benefit compared to when more hearing was preserved. Music perception performance using the Hybrid L24 did not, on average, change compared to hearing-aided baseline, although individual performance appeared to again relate to the amount of preserved residual hearing. Six study subjects opted to be explanted and reimplanted with a traditional cochlear implant due to reasons that include hearing loss and dissatisfaction. The risks associated with the device, including residual low-frequency hearing loss and the risk of explantation/reimplantation should therefore be carefully

considered by potential candidates and their hearing health-care providers. However, FDA believes that the available data demonstrate that the benefits outweigh these risks in the pivotal study patient population, particularly since the device provided speech-understanding benefit for most subjects, including even the majority of individuals who lost residual hearing to the profound levels.

XIV. CDRH DECISION

CDRH issued an approval order on March 20, 2014. The final conditions of approval cited in the approval order are described below.

***Extended Follow-up Study**:* This study is an extended follow-up of the subjects who were enrolled in the pivotal study to assess long-term device performance. The study will be conducted as a prospective, non-controlled, non-randomized, multicenter study at the 10 sites. All 39 available subjects who were enrolled in the pivotal study will be invited to participate in the extended follow-up. Study subjects will be followed for 5 years post-implantation of the device. The primary safety endpoint is the comparison of the type and frequency of adverse events and serious adverse events observed during the duration of the study compared to the pivotal study. The effectiveness endpoints will include the within-subject differences for the two speech recognition tests, i.e., word recognition in quiet as evaluated with the Consonant-Nucleus-Consonant (CNC) test, and sentence recognition in noise as evaluated with the AzBio test (+5dB SNR). The change in the perceived hearing benefits, patient satisfaction with the device use and quality of life will be assessed by employing patient reported questionnaires. Follow-up will occur at 36, 48 and 60 months post-implantation. Every explanted device will be tested to determine the reason for device failure, and device explantations will be reported as serious adverse events.

***New Enrollment Study**:* The purpose of this study is to provide longer-term data on the safety and effectiveness of the Nucleus Hybrid L24 Cochlear Implant System under general conditions of use in the postmarket environment. This study will be conducted as a prospective, non-controlled, non-randomized study in 25 clinical sites. A total of 100 subjects newly treated will be enrolled. Study subjects will be followed for 5 years post-implantation of the device with a target follow-up rate of 80% at the end of the study. The primary safety endpoint is the comparison of the type and frequency of adverse events and serious adverse events observed during the duration of the study compared to the pivotal study. The effectiveness endpoints will include the within-subject differences for the two speech recognition tests, i.e., word recognition in quiet as evaluated with the Consonant-Nucleus-Consonant (CNC) test, and sentence recognition in noise as evaluated with the AzBio test (+5dB SNR). The change in the perceived hearing benefits, patient satisfaction with the device use and quality of life will be assessed by employing patient reported questionnaires. Follow-up will occur at 3, 6, 12, 24, 36, 48 and 60 months post-implantation. Every explanted device will be tested to determine the reason for device failure, and device explantations will be reported as serious adverse events.

The applicant's manufacturing facility has been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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Cochlear™

Nucleus® Hybrid™ L24 cochlear implant

CI24REH

Professional Package Insert

Hear now. And always

Cochlear®

Symbols

Note

Important information or advice. Can avoid inconvenience.

Caution

Special care to be taken to ensure safety and effectiveness.

Could cause damage to equipment.

Warning (harmful)

Potential safety hazards and serious adverse reactions.

Could cause harm to person.

This document contains important information such as indications and contraindications that apply to the following cochlear implant systems:

- Cochlear™ Nucleus® Hybrid™ L24 cochlear implant (CI24REH)

Caution

Federal law restricts this device to sale by or on the order of a physician.

Contents

Notes

Glossary

- Everyday Listening Condition – The use of the Cochlear Nucleus Hybrid cochlear implant system in conjunction with a hearing aid in the other ear.
- Cochlear Nucleus Hybrid cochlear implant system – The Cochlear Nucleus Hybrid L24 cochlear implant and Nucleus 6 Sound Processor including coil/cable, battery module, and Remote Assistant, used with or without the acoustic component.
- Implant Ear Alone Condition – The use of the Cochlear Nucleus Hybrid cochlear implant system with no sound input from the other ear or the use of electric hearing with the available low-frequency hearing in the same ear.
- Functional Acoustic Hearing – Acoustic (rather than electric) hearing of a severe degree or better (<90dB).
- Nonfunctional Acoustic Hearing – Acoustic (rather than electric) hearing of a profound degree (≥90dB).

Device description

The Cochlear Nucleus Hybrid L24 cochlear implant system is an electric-acoustic (E+A) stimulation system intended to address the needs of individuals who demonstrate normal to moderate low-frequency hearing loss and severe to profound mid- and high-frequency sensorineural hearing loss.

The Cochlear Nucleus Hybrid L24 system includes both implanted and external components. The implanted components of the system are:

- The Cochlear Nucleus Hybrid L24 cochlear implant consisting of the Cochlear Nucleus CI24RE receiver/stimulator assembly with the Hybrid L24 electrode array. The implant is provided sterile.

The external components are non-sterile and include:

- The Cochlear Nucleus 6 (N6) sound processor with coil/cable, battery module, acoustic component and accessories
- Two user options for Remote Assistants.

Information for use and recommended training

Physicians should be very experienced in mastoid surgery and the facial recess approach to the oval window and round window. It is important that physicians be trained in the implantation procedure for the Cochlear Nucleus Hybrid L24 cochlear implant. It is strongly recommended that the surgeon work with an experienced team of audiology, speech-language, rehabilitation, education and psychology professionals. It is recommended that audiology professionals attend a training program for this device.

Cochlear Americas conducts periodic training courses. For product-specific information, refer to the Surgeon's Guide supplied with each implant.

Indications for use

The Cochlear Nucleus Hybrid L24 cochlear implant system is intended to provide electric stimulation to the mid- to high-frequency region of the cochlea and acoustic amplification to the low-frequency regions, for patients with residual low-frequency hearing sensitivity.

The system is indicated for unilateral use in patients aged 18 years and older who have residual low-frequency hearing sensitivity and severe to profound high-frequency sensorineural hearing loss, and who obtain limited benefit from appropriately fitted bilateral hearing aids.

Typical preoperative hearing of candidates ranges from normal to moderate hearing loss in the low frequencies (thresholds no poorer than 60 dB HL up to and including 500 Hz), with severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥75 dB HL) in the ear to be implanted, and moderately severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥ 60 dB HL) in the contralateral ear.

The CNC word recognition score will be between 10% and 60%, inclusively, in the ear to be implanted in the preoperative aided condition and in the contralateral ear will be equal to or better than that of the ear to be implanted but not more than 80% correct.

Prospective candidates should go through a suitable hearing aid trial, unless already appropriately fitted with hearing aids.

Contraindications

A Cochlear Nucleus Hybrid L24 cochlear implant is not indicated for individuals who have the following conditions:

1. Deafness due to lesions of the acoustic nerve or central auditory pathway
2. Active middle ear disease, with or without tympanic membrane perforation
3. Absence of cochlear development
4. A duration of severe to profound hearing loss of 30 years or greater.

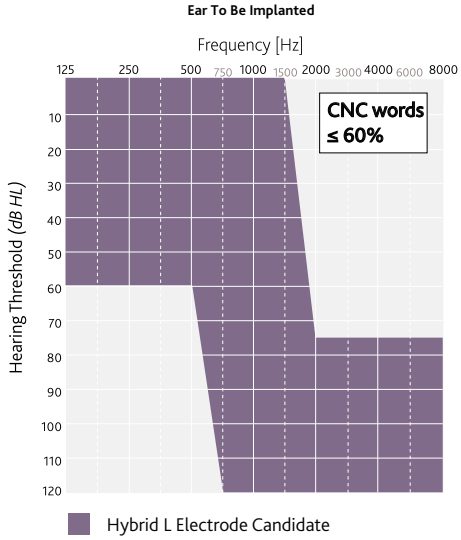

Figure 1: Shaded audiogram depicting the indicated thresholds for Cochlear Nucleus Hybrid L24 candidacy in the ear to be implanted

⚠ Warnings

Medical treatments generating induced currents

Below are some some medical treatments that generate induced currents which may cause tissue damage or permanent damage to the implant.

Electrosurgery

Electrosurgical instruments are capable of inducing radio frequency currents that could flow through the electrode array. Monopolar electrosurgical instruments must not be used on the head or neck of an implant patient as induced currents could cause damage to cochlear tissues or permanent damage to the implant. Bipolar electrosurgical instruments may be used on the head and neck of patients; however, the cautery electrodes must not contact the implant and should be kept more than 1 cm (~0.5 in.) from the extracochlear electrodes.

Diathermy

Do not use therapeutic or medical diathermy (thermopenetration) using electromagnetic radiation (magnetic induction coils or microwave). High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant. Medical diathermy using ultrasound may be used below the head and neck.

Neurostimulation

Do not use neurostimulation directly over the implant. High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant.

Electroconvulsive therapy

Do not use electroconvulsive therapy on an implant patient under any circumstances. Electroconvulsive therapy may cause tissue damage to the cochlea or damage to the implant.

Ionizing radiation therapy

Do not use ionizing radiation therapy directly over the implant because it may cause damage to the implant.

Magnetic Resonance Imaging (MRI)

MRI is contraindicated for patients with the Cochlear Nucleus Hybrid cochlear implant.

Meningitis

Prior to implantation, candidates should be instructed to consult their primary care physician and implanting surgeon regarding their vaccination status against organisms that cause meningitis. Meningitis is a known risk of inner ear surgery and candidates should be appropriately counselled of this risk.

In addition, certain pre-operative conditions may increase the risk of meningitis with or without an implant. These conditions include:

- Mondini's syndrome and other congenital cochlear malformations
- Concurrent Cerebrospinal Fluid (CSF) shunts or drains
- Recurrent episodes of bacterial meningitis prior to implantation
- Perilymph fistulas and skull fracture/defect with CSF communication.

Hearing sensitivity

At six months postactivation most individuals (90%) retain a level of acoustic hearing and many (66%) utilize that hearing with or without amplification at the implant ear. For some individuals, a total loss of functional acoustic hearing in the implanted ear may occur. See the Safety Analysis section for additional information. Changes in low frequency hearing sensitivity at the six month study endpoint are summarized below:

- 33 subjects (66%) maintained hearing of a severe degree or better, referred to as functional acoustic hearing
- 17 (34%) experienced a decrease in low frequency hearing resulting in profound loss of hearing, referred to as nonfunctional acoustic hearing.

There is limited long-term data available on the effects of Cochlear Hybrid implantation on hearing sensitivity. Following the six month study endpoint, five additional subjects experienced a decrease in low frequency hearing resulting in profound loss of hearing, with the loss occurring up to 48 months post-surgery.

Long term effects of electrical stimulation

Most patients can benefit from electrical stimulation levels that are considered safe, based on animal experimental data. For some patients, the levels needed to produce the loudest sounds exceed these levels. The long-term effects of such stimulation in humans are unknown.

Small parts hazard

Patients and caregivers should be counseled that the external implant system contains small parts that may be hazardous if swallowed or may cause choking if inhaled.

Head trauma

A blow to the head in the area of the implant may damage the implant and result in its failure. For recommendations on how to minimize the chance of experiencing head trauma, patients should refer to http://www.cdc.gov/ncipc/pub-res/tbi_toolkit/patients/preventing.htm

Use of batteries and battery ingestion

When using disposable batteries, patients should be instructed to only use battery types recommended by Cochlear. Other types may not have sufficient energy to allow the processor to operate for a long time. Cochlear does not recommend the use of silver oxide or alkaline batteries.

Batteries can be harmful if swallowed. Ensure that batteries are kept out of reach of young children and pets. If swallowed, patients should seek prompt medical attention at the nearest emergency center.

Rechargeable batteries

In certain circumstances, rechargeable batteries can become VERY HOT and could cause injury. The processor should be removed immediately if it becomes unusually warm or hot, and a clinician consulted for advice. Caregivers should be instructed to touch their recipient's processor to check for heat if the recipient is showing signs of discomfort. Rechargeable batteries should NEVER be worn beneath clothing (including scarves and headwear covering the ears). The rechargeable battery should not be used by patients who cannot remove the device themselves, or notify a caregiver that the device has become hot.

Overheating of external devices

Patients should be cautioned to remove the processor immediately if it becomes unusually warm or hot, and seek advice from a clinician. Caregivers should be instructed to touch their recipient's processor to check for heat if the recipient is showing signs of discomfort. The manufacturer only recommends the use of Cochlear rechargeable battery modules and zinc air disposable batteries. The processor is not intended to be used with silver oxide batteries. In some circumstances, the use of these batteries could result in severe burns. A dangerous amount of heat can be generated by these batteries in conditions where heat cannot dissipate, especially if the device is being held against the skin by clothing or a retention device. In addition, use of silver oxide batteries may damage the processor.

⚠ Precautions

If the recipient experiences a significant change in performance or the sound becomes uncomfortable, they should be instructed to turn off the processor and contact the implant center.

The cochlear implant system should be used only with the approved devices and accessories listed in the user guide.

The processor and other parts of the system contain complex electronic parts. These parts are durable but must be treated with care. The processor must not be opened by anyone other than Cochlear's qualified service personnel or the warranty will be invalidated.

Each processor is programmed specifically for each implant. Recipients should never wear another person's processor or lend theirs to another user. Using the wrong processor could result in loud or distorted sounds that, in some instances, may cause extreme discomfort.

The processor should not be operated at temperatures above +40 °C (+104 °F) or less than +5 °C (+41 °F).

The processor should not be stored at temperatures above +50 °C (+122 °F) or less than -20 °C (-4 °F).

The processor's sound quality may be intermittently distorted when it is within approximately 1.6 km or 1 mile of a radio or television transmission tower. Additional sources of interference include, but are not limited to:

- Security systems
- Industrial machinery and power systems
- Mobile communications equipment (including cellular telephones)
- Certain kinds of hand-held, two-way radios (including Citizen Band, Family Radio Service, and Amateur Band).

To reduce or eliminate the interference, the recipient should move the processor away from the source. If the processor stops working, the recipient should turn the power switch off and then back on. This effect is temporary and will not damage the processor.

Storage, handling and sterilization

Implants should be stored at normal room temperature. Implants may be stored at temperatures between -4 °F and +120 °F (-20 °C and +50 °C). The 'use by' date is stamped on the outside package. If it has expired, return the device to Cochlear. Handle the implant packages with care. Severe impact may rupture the inner sterile package. Cochlear implants are supplied sterile in gas-permeable packaging. The titanium plugs and replacement magnets are supplied separately in sterile gas-permeable packaging. These are single use items. The sterile package contains information indicating ethylene oxide processing. Before opening the sterile package, inspect it carefully. If the package is ruptured, or exposure to ethylene oxide processing is not indicated, please return the package to Cochlear.

Theft and metal detection systems

Devices such as airport metal detectors and commercial theft detection systems produce strong electromagnetic fields. Some cochlear implant recipients may experience a distorted sound sensation when passing through or near one of these devices. To avoid this, the recipient should turn off the processor when in the vicinity of one of these devices. The materials used in the cochlear implant may activate metal detection systems. For this reason, recipients should carry the Cochlear Implant Patient Identification Card with them at all times.

Electrostatic discharge

A discharge of static electricity can damage the electrical components of the cochlear implant system or corrupt the program in the processor. If static electricity is present (e.g. when putting on or removing clothes over the head or getting out of a vehicle), cochlear implant recipients should touch something conductive (e.g. a metal door handle) before the cochlear implant system contacts any object or person. Prior to engaging in activities that create extreme electrostatic discharge, such as playing on plastic slides, the processor should be removed. Clinicians should use an anti-static shield on the computer monitor when programming a cochlear implant recipient.

Mobile telephones

Some types of digital mobile telephones (e.g. Global System for Mobile communications (GSM) as used in some countries) may interfere with the operation of the external equipment. As a result, cochlear implant recipients may perceive a distorted sound sensation when in close proximity, 1–4 m (~3–12 ft), to a digital mobile telephone in use.

Scuba diving

Implant Type	Maximum depth
CI24REH Implant	40m (~131 ft)

Table 1: Maximum diving depths when wearing implants

The Sound Processor must be removed before diving. Recipients should seek medical advice before participating in a dive for conditions that might make diving contraindicated, for example middle ear infection, etc. When wearing a mask, avoid pressure over the implant site.

Sleeping

Recipients should not wear the processor while sleeping, as they may not become aware of the processor becoming unusually warm or hot.

Retention aids

When using retention aids such as the Snugfit™ or LiteWear, be aware that it may take longer to remove the processor if the processor becomes unusually warm or hot.

Do not attach the LiteWear beneath layers of clothing.

Electromagnetic interference with medical devices

Cochlear Nucleus Remote Assistants meet defined international Electromagnetic Compatibility (EMC) and emission standards. However, because the remote assistant radiates electromagnetic energy, it is possible that it could interfere with other medical devices such as cardiac pacemakers and implantable defibrillators when used nearby. It is recommended that the Remote Assistant is kept at least 6 in. (~15.2 cm) away from devices which could be subject to electromagnetic interference. For added assurance, recipients should also consult the recommendations provided by the device manufacturer.

Electromagnetic Compatibility (EMC)

Guidance and manufacturer's declaration

The Cochlear Nucleus Series Sound Processor and Remote Assistant are intended for use in the electromagnetic environments specified in this document.

They have been tested and found to be in compliance as shown. Recipients should take care to use the processor as described.

Electromagnetic emissions

Emission test	Compliance	Guidance
RF emissions CISPR 11	Group 1	RF energy is only used for its internal function. The RF emissions are very low and not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The device is suitable for use in all establishments, including domestic establishments and those directly connected to public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable	
Voltage fluctuations/flicker emissions IEC 61000-3-3		

Table 2: Electromagnetic emissions

Electromagnetic immunity

Immunity test	IEC 60601 test level	Compliance level	Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±6 kV contact ±8 kV air	±6 kV contact ±8 kV air	See ***Electrostatic discharge*** on page page 17
Electrical fast transient/burst IEC 61000-4-4	Not applicable		
Surge IEC 61000-4-5			
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11			
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields be at levels characteristic of a typical location in a typical commercial or hospital environment
Conducted RF IEC 61000-4-6 Radiated RF IEC 61000-4-3	Not applicable 3 V/m 80 MHz to 2.5 GHz	3 V/m	See the ***Warnings*** and ***Precautions*** sections, and ***Guidance*** below

Table 3: Electromagnetic immunity

Guidance

Portable and mobile RF communications equipment should be used no closer to any part of the devices, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.

Recommended separation distance (d):

$d = 1.2\sqrt{P}$ 80 MHz to 800 MHz

$d = 2.3\sqrt{P}$ 800 MHz to 2.5 GHz

where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in metres (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey[a], should be less than the compliance level in each frequency range[b].

Interference may occur in the vicinity of equipment marked with the following symbol.

Note

1. At 80 MHz and 800 MHz, the higher frequency range applies.
2. These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Explanatory notes:

a. Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the processor is used exceeds the applicable RF compliance level above, the processor should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the processor.

b. Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

Recommended separation distances

Your processor is intended for use in an electromagnetic environment where the radiated RF disturbances are controlled.

To prevent electromagnetic interference, maintain a minimum distance between the portable and mobile RF communications equipment (transmitters) and the device as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (W)	Separation distance according to frequency of transmitter (m)		
	150 kHz to 80 MHz $d = 1.2\sqrt{P}$	80 MHz to 800 MHz $d = 1.2\sqrt{P}$	800 MHz to 2.5 GHz $d = 2.3\sqrt{P}$
0.01	Not applicable	0.12	0.23
0.1		0.38	0.73
1		1.2	2.3
10		3.8	7.3
100		12	23

Table 4: Recommended separation distances

For transmitters rated at a maximum output power not listed above, the recommended separation distance d in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

Note

1. At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.
2. These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Clinical trial description

The objective of this multicenter, pivotal study was to evaluate the safety and effectiveness of the Cochlear Nucleus Hybrid L24 cochlear implant system. Participants in the study had sensorineural hearing loss, characterized by a normal through moderate range in the low frequencies and a severe to profound loss in the high frequencies. Subjects were assessed with and without use of an additional hearing aid in the contralateral (unimplanted) ear. When testing the implant ear alone, subjects made use of electric hearing and whatever low frequency hearing they had available to them in the same ear. Since participants made use of the device in conjunction with a hearing aid in the contralateral ear, speech perception was also measured in this, Everyday, listening condition.

Individual audiometric data were examined across test intervals to measure any changes in hearing sensitivity and to understand the impact of the procedure on hearing sensitivity in the low frequencies.

The co-primary endpoints of the study were based on a comparison of the change in average speech perception scores (both in quiet and in noise) between the preoperative and 6-month time points in the implanted ear alone with the patients utilizing electric hearing and whatever low frequency hearing was available in the implanted ear.

Secondary endpoints assessed the proportion of subjects who experienced statistically significant improvements on speech performance measures in the implanted ear.

Subject demographics and accountability

Key demographics are shown in Table 5 below.

Demographic Characteristics	Mean ± SD N (min, max)
Age at CI in Years	64.1 ± 14.7 50 (23.0 – 86.2)
Duration of Overall Hearing Loss in Years	28.1 ± 14.9 50 (3.4 – 73.9)
Duration of High Frequency Hearing Loss in Years	13.1 ± 7.2 50 (1.6 – 30.1*)
Male	25/50 (50.0%)
Female	25/50 (50.0%)
Pre-operative Degree of LF PTA (Implanted Ear):	
Normal (0 – 25 dB HL)	1/50 (2.0%)
Mild (26 - 40 dB HL)	13/50 (26.0%)
Moderate (41 – 55 dB HL)	26/50 (52.0%)
Moderate-Severe (56 – 70 dB HL)	10/50 (20.0%)

* One subject met the requirement of < 30 years duration of severe to profound high frequency loss at candidacy assessment but was slightly over 30 years duration by the time surgery was approved for reimbursement and completed.

Table 5: Demographics for the 50 study subjects

Fifty subjects were enrolled and implanted among the investigative sites. Forty-nine of these subjects completed the six month evaluation. One subject was reimplanted with a full length array due to poor performance and loss of hearing sensitivity, and did not complete the six month evaluation. Of these forty-nine subjects, two completed only speech performance and SSQ measures, and one completed only speech perception measures, due to time constraints and clinician preference.

Study inclusion and exclusion criteria

Individuals who presented with the previously described hearing loss and met the specific inclusion/exclusion criteria were included in the study.

Criteria for Inclusion:

1. Eighteen years of age or older at the time of implantation.
2. Severe to profound (a threshold average of 2000, 3000, & 4000 Hz ≥ 75dB HL) sensorineural hearing loss for frequencies > 1500 Hz. Low frequency thresholds up to and including 500 Hz should be no poorer than 60 dB HL.
3. CNC word recognition score (mean of two lists) between 10% and 60%, inclusive (i.e., 10% ≤ score ≤ 60%), in the ear to be implanted.
4. CNC word recognition score in the contralateral ear equal to, or better than, the ear to be implanted but not more than 80%.
5. English spoken as a primary language.

Criteria for exclusion:

1. Duration of severe to profound hearing loss > 30 years.
2. Congenital hearing loss (for the purpose of this study, onset prior to 2 years of age).
3. Medical or psychological conditions that contraindicate undergoing surgery.
4. Ossification or any other cochlear anomaly that might prevent complete insertion of the electrode array.
5. Conductive overlay of 15 dB or greater at two or more frequencies, in the range 250 to 1000 Hz.
6. Hearing loss of neural or central origin.
7. Diagnosis of Auditory Neuropathy.
8. Active middle ear infection.
9. Unrealistic expectations on the part of the subject, regarding the possible benefits, risks, and limitations that are inherent to the surgical procedure(s) and prosthetic devices.
10. Unwillingness or inability of the candidate to comply with all investigational requirements.
11. Additional handicaps that would prevent or restrict participation in the audiological evaluations.

Description of tests

CNC Monosyllabic Word Recognition Test (Primary endpoint)

The CNC Monosyllabic Word Recognition Test is a measure of open-set word recognition consisting of 10 recorded lists of 50 monosyllabic words (consonant-nucleus-consonant) such as 'laud' and 'duck'. Two lists were administered in quiet at 60 dBA in the sound field and reported as percent correct for words and phonemes.

AzBio Sentence Test (Primary endpoint)

The AzBio Sentence Test is a measure that consists of 33 lists of 20 sentences (such as 'He cried when the pet goat was sent to market.') that contain low contextual information. Each list includes 5 sentences from each of four different speakers (two male, two female). Two lists of the AzBio sentences were presented at 60 dBA with competing noise (babble) presented at a level to achieve a +5 dB signal-to-noise ratio from the same loudspeaker.

University of Washington Clinical Assessment of Music Perception (UW-CAMP)

The UW-CAMP test consists of three subtests each designed to provide an assessment of fundamental auditory skills important for music perception. The three subtests were presented at 65 dBA and provided an assessment of pitch perception, melody recognition and timbre.

The Speech, Spatial, and Qualities of Sound Questionnaire (SSQ)

The SSQ is a validated self-assessment metric commonly used in hearing aid and cochlear implant research. It is designed to measure self-reported auditory disability across a wide variety of domains, reflecting the reality of hearing in the everyday world. There are 49 questions scored by the subject using a scale of 0 through 10, where 0 corresponded to minimal ability and 10 corresponded to complete ability. There are three specific hearing domains assessed:

- Speech hearing scale – hearing speech in quiet and in noise, one-on-one conversation and in groups/meetings
- Spatial hearing scale – hearing where sounds are coming from, distance, movement, and ability to segregate sounds
- Qualities of sound scale – ease of listening, naturalness, clarity, identification of different speakers, musical pieces and instruments as well as everyday sounds.

Device Use Questionnaire (DUQ)

This questionnaire (~90 questions) was developed by Cochlear and is used to collect information regarding device usability, subjective preferences and satisfaction with regards to device use in various listening conditions. The questions summarized in this document are those related to patient satisfaction; excluded questions centered around descriptions of device use by the study subjects.

Clinical trial results

Speech perception

Implant Ear Alone Condition (Co-Primary Endpoints)

Understanding Speech in Quiet – CNC Monosyllabic Word Test

Forty-nine of fifty subjects had CNC word recognition scores available pre- and post-operatively after six months of experience using the Nucleus Hybrid L24 cochlear implant in the Implant Ear Alone condition.

- Average performance after six months experience with the Implant Ear Alone condition was significantly higher than average performance for the subjects using a hearing aid prior to implantation.
  - Average CNC scores were 28.4% (9% - 64%) pre-operatively with one hearing aid and 65.4% (8% - 98%) at six months in the Implant Ear Alone condition for the 49 subjects.

Note

Data presented in this section does not include interpolation for the one subject who did not complete the primary study endpoint.

Understanding Speech in Noise – AzBio Sentence Test in Noise (+5 dB SNR)

Forty-nine of fifty subjects had AzBio sentence recognition in noise (+5 dB SNR) scores available pre- and post-operatively after six months of experience using the Cochlear Nucleus Hybrid L24 cochlear implant in the Implant Ear Alone condition.

- Average performance after six months experience with the Implant Ear Alone condition was significantly higher than average performance for the subjects using one hearing aid prior to implantation.
  - Average AzBio sentences in noise scores were 16.3% (0.0% - 64.1%) pre-operatively with one hearing aid and 49.2% (0.0% - 91.5%) at six months in the Implant Ear Alone condition for the 49 subjects.

Additional test measures – Everyday Listening condition

Understanding Speech in Quiet – CNC Monosyllabic Word Test

Forty-nine of fifty subjects had CNC word recognition scores available pre- and post-operatively after six months of experience using the Nucleus Hybrid L24 cochlear implant in the Everyday Listening condition.

- Average performance after six months experience with the Everyday Listening condition was significantly higher than average performance for the subjects using two hearing aids prior to implantation.
  - Average CNC scores were 44.9% (2% - 81%) pre-operatively with two hearing aids and 79.4% (35% - 98%) at six months in the Everyday Listening condition for the 49 subjects.
- After six months of experience using the Everyday Listening condition:
  - All subjects (49/49; 100%) demonstrated similar or better word recognition (CNC) compared with their pre-operative performance using two hearing aids.
  - Most (43/49; 87.8%) demonstrated significantly better word recognition compared with their pre-operative performance using two hearing aids.
- Approximately half of the recipients recognized 84.0% or more of the words (CNC) and approximately three quarters recognized 67.0% or more words after six months experience in the Everyday Listening condition.

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Understanding Speech in Noise – AzBio Sentence Test in Noise (+5 dB SNR)

Forty-nine of fifty subjects had AzBio sentence recognition in noise (+5 dB SNR) scores available pre- and post-operatively after six months of experience using the Cochlear Nucleus Hybrid L24 cochlear implant in the Everyday Listening condition.

- Average performance after six months experience with the Everyday Listening condition was significantly higher than average performance for the subjects using two hearing aids prior to implantation.
  - Average AzBio sentences in noise scores were 29.6% (0.0% - 76.5%) pre-operatively with two hearing aids and 62.6% (3.6% - 92.7%) at six months in the Everyday Listening condition for the 49 subjects.
- After six months of experience using the Everyday Listening condition:
  - Most recipients (49/49; 100%) demonstrated similar or better sentence recognition in noise (AzBio) compared with their pre-operative performance using two hearing aids
  - Most (41/49; 84%) demonstrated significantly better sentence recognition in noise (AzBio) compared with their pre-operative performance using two hearing aids.
- Approximately half of the recipients recognized 71.6% or more of the words in a sentence when in background noise and approximately three quarters recognized 43.4% or more of the words in a sentence in background noise after six months experience in the Everyday Listening condition.

Proportion of subjects demonstrating similar performance or improved performance

As shown in Table 6, the secondary endpoints were met and exceeded for both metrics, as most (> 75%) of the subjects scored equal to or better than they did in the preoperative Unilateral Acoustic-Only condition. Though it was not a primary or secondary endpoint, when the Everyday Mode at six months is considered in the analysis, an even higher proportion of subjects showed significant improvement. Additionally, Table 7 shows the proportion of subjects with post-operative scores better than those obtained pre-operatively by the six month study interval.

Listening Mode	CNC Words	CNC Phonemes	AzBio in Noise
Implant Ear Alone (Study Endpoint)	96.0%	91.8%	89.8%
Everyday Condition	100%	100%	100%

Table 6: Proportion of subjects with post-operative score equal to or better than pre-operative at the six month study interval

Listening Mode	CNC Words	CNC Phonemes	AzBio in Noise
Implant Ear Alone (Study Endpoint)	81.6%	85.7%	73.5%
Everyday Condition	87.8%	89.9%	83.7%

Table 7: Proportion of subjects with post-operative score better than pre-operative at the six month study interval

Music performance - University of Washington Clinical Assessment of Music Perception (UW-CAMP)

Everyday Listening condition

Forty-six of fifty subjects had Pitch Discrimination scores available pre- and post-operatively after six months of experience using the Cochlear Nucleus Hybrid L24 cochlear implant in the Everyday Listening condition.

Pitch Discrimination

- Average pitch discrimination ability was similar to that observed for normally hearing individuals.[1]
- Performance remained unchanged pre-operatively with two hearing aids to post-operatively at six months in the Everyday Listening condition.
  - Average pitch discrimination was 1.1 (0.5 – 6.3) semitones pre-operatively compared to 1.1 (0.5 – 3.7) semitones at six months for the 46 subjects.
- After six months of experience using the Everyday Listening condition:
- Most recipients (42/46; 91.3%) demonstrated similar (within 1 semitone) or better pitch discrimination compared with their pre-operative performance using two hearing aids.
- Pitch discrimination ranged from 0.5 to 3.7 semitones after six months experience in the Everyday Listening condition.
- Approximately half of the recipients had pitch discrimination of 0.7 semitones or better and approximately three-quarters had pitch discrimination of 1.5 semitones or better after six months experience in the Everyday Listening condition.

1 Kang, S.Y., Nimmons, G.L., Drennan, W., Longnion, J., Ruffin, C., Nie, K., Won, J.H., Worman, T., Yueh, B., Rubinstein, J. (2009). Development and validation of the University of Washington clinical assessment of music perception test. *Ear Hear*, 30(4), 411-418.

Implant Ear Alone condition

Forty-six of fifty subjects had Pitch Discrimination scores available pre- and post-operatively after six months of experience using the Cochlear Nucleus Hybrid L24 cochlear implant in the Implant Ear Alone condition.

Pitch Discrimination

- Average performance remained relatively unchanged pre-operatively with one hearing aid to post-operatively at six months in the Everyday Listening condition
  - Average pitch discrimination was 1.1 (0.5 – 4.8) semitones pre-operatively compared to 1.5 (0.5 – 8.9) semitones at six months for the 46 subjects.
- After six months of experience using the Implant Ear Alone listening condition:
- Most recipients (42/46; 91.3%) demonstrated similar (within 1 semitone) or better pitch discrimination compared with their pre-operative performance using one hearing aid.
- Pitch discrimination ranged from 0.5 to 8.9 semitones after six months experience in the Implant Ear Alone condition.
- Approximately half of the recipients had pitch discrimination of 0.9 semitones or better and approximately three-quarters had pitch discrimination of 1.8 semitones or better after six months experience in the Everyday Listening condition.

Device Use Questionnaire – Music

- When compared to pre-operative levels, satisfaction improved across all six music/sound quality related areas at the six month interval.
  - When listening to live music with singing, satisfaction increased from 8.5% to 53.3%
  - When listening to live music without singing, satisfaction increased from 42.6% to 62.2%
  - When listening to recorded music with singing, satisfaction increased from 6.0% to 57.4%
  - When listening to recorded music without singing, satisfaction increased from 28.6% to 66.0%
  - When listening to music in general, satisfaction increased from 26.0% to 58.3%.

Self-assessment – Everyday Listening condition

Speech, Spatial, and Qualities of Hearing (SSQ) Scale

Forty-eight of fifty subjects had SSQ ratings available pre- and post-operatively after six months of experience using the Cochlear Nucleus Hybrid L24 cochlear implant in the Everyday Listening condition.

Speech Hearing Rating Scale

For this scale subjects answered questions concerning how well they heard and understood speech in various quiet and noisy situations involving one-on-one conversations and communication in small and large groups of people. The subject rated their ability to hear on a scale from 1 to 10, where 1 represented the poorest rating possible and 10 represented the best rating possible. A difference in a rating of 1 to 2 was indicative of a change in self-perceived benefit. Changes of more than 2 and less than 4 were indicative of high self-perceived benefit with changes of 4 or more indicative of very high self-perceived benefit.

- Average performance after six months experience with the Everyday listening condition was significantly higher than average performance for the subjects using two hearing aids prior to implantation.
  - Average SSQ ratings for the Speech Hearing Scale were 3.2 (0.8 – 6.2) out of 10 pre-operatively with two hearing aids and 5.4 (0.7 – 8.8) out of 10 at six months in the Everyday listening condition for the 48 subjects.
- After six months of experience using the Everyday Listening condition:
  - Most recipients (45/48; 93.8%) demonstrated similar or better ratings for the Speech Hearing Scale compared with their pre-operative performance using two hearing aids
  - Most (37/48; 77.1%) reported benefit to very high benefit on the Speech Hearing Scale compared with their pre-operative performance using two hearing aids.
    - 3/48 (6.3%) reported a negative benefit rating
    - 8/48 (16.7%) reported no change on the Speech Hearing Scale

- 11/48 (22.9%) reported benefit (1 to 2) on the Speech Hearing Scale
- 20/48 (41.7%) reported high benefit (2 to 4) on the Speech Hearing Scale
- 6/48 (12.5%) reported very high benefit (4 or more) on the Speech Hearing Scale.

Spatial Hearing Rating Scale

For this scale subjects answered questions concerning how well they could judge where a sound was coming from, how far away the sound was, and movement of sound (e.g., whether a sound was coming toward them or away from them). The subject rated their ability to hear on a scale from 1 to 10, where 1 represented the poorest rating possible and 10 represented the best rating possible. A difference in a rating of 1 to 2 was indicative of a change in self-perceived benefit. Changes of more than 2 and less than 4 were indicative of high self-perceived benefit with changes of 4 or more indicative of very high self-perceived benefit.

- Average performance after six months experience with the Everyday Listening condition was significantly higher than average performance for the subjects using two hearing aids prior to implantation.
  - Average SSQ ratings for the Spatial Hearing Scale were 4.6 (1.4 – 9.2) out of 10 pre-operatively with two hearing aids and 5.5 (1.1 – 8.3) out of 10 at six months in the Everyday Listening condition for the 48 subjects.

- After six months of experience using the Everyday Listening condition:
  - Most recipients (39/48; 81.3%) demonstrated similar or better ratings for the Spatial Hearing Scale compared with their pre-operative performance using two hearing aids
  - Many (26/48; 54.2%) reported benefit to very high benefit on the Speech Hearing Scale compared with their pre-operative performance using two hearing aids.
    - 9/48 (18.8%) reported a negative benefit rating
    - 13/48 (27.1%) reported no change on the Spatial Hearing Scale
    - 12/48 (25.0%) reported benefit (1 to 2) on the Spatial Hearing Scale
    - 13/48 (27.1%) reported high benefit (2 to 4) on the Spatial Hearing Scale
    - 1/48 (2.1%) reported very high benefit (4 or more) on the Spatial Hearing Scale.

Sound Qualities Rating Scale

For this scale subjects answered questions concerning how well they could separate and sort out sounds, how well they could recognize different sounds, how clear or natural sounds were, and how much effort listening required. The subject rated their ability to hear on a scale from 1 to 10, where 1 represented the poorest rating possible and 10 represented the best rating possible. A difference in a rating of 1 to 2 was indicative of a change in self-perceived benefit. Changes of more than 2 and less than 4 were indicative of high self-perceived benefit with changes of 4 or more indicative of very high self-perceived benefit

- Average performance after six months experience with the Everyday Listening condition was significantly higher than average performance for the subjects using two hearing aids prior to implantation.
  - Average SSQ ratings for the Sound Qualities Scale were 5.0 (1.6 – 8.1) out of 10 pre-operatively with two hearing aids and 6.3 (2.7 – 9.1) out of 10 at six months in the Everyday Listening condition for the 48 subjects.
- After six months of experience using the Everyday Listening condition:
  - Most recipients (43/48; 89.6%) demonstrated similar or better ratings for the Sound Qualities Scale compared with their pre-operative performance using two hearing aids
  - Many (28/48; 58.3%) reported benefit to very high benefit on the Sound Qualities Scale compared with their pre-operative performance using two hearing aids.
    - 5/48 (10.4%) reported a negative benefit rating
    - 15/48 (31.3%) reported no change on the Sound Qualities Scale
    - 8/48 (16.7%) reported benefit (1 to 2) on the Sound Qualities Scale
    - 16/48 (33.3%) reported high benefit (2 to 4) on the Sound Qualities Scale
    - 4/48 (8.3%) reported very high benefit (4 or more) on the Sound Qualities Scale.

Device Use Questionnaire

- When compared to pre-operative levels, overall satisfaction increased at the six month interval.
  - The number of subjects satisfied with their performance increased from 8.0% to 79.2%.
- When compared to pre-operative levels, satisfaction improved across all seven listening situations at the six month interval.
  - When listening using a telephone, satisfaction increased from 10.0% to 29.2%
  - When listening in a noisy environment, satisfaction increased from 0.0% to 33.3%
  - When listening in a quiet environment, satisfaction increased from 34.0% to 85.4%
  - When listening in a one-on-one situation, satisfaction increased from 44.0% to 93.8%
  - When listening in a small group situation, satisfaction increased from 16.0% to 75.0%
  - When listening in a large group situation, satisfaction increased from 2.0% to 45.8%
  - When listening to a source at a distance (in church, at a music hall), satisfaction increased from 6.0% to 50.0%
  - When listening to the outdoors (birds, nature sounds, etc.), satisfaction increased from 32.7% to 83.0%.

Safety analysis

Hearing sensitivity

This study involved implanting subjects with functional low frequency hearing. Changes in hearing sensitivity were assessed and those that resulted in profound (> 90 dB HL) loss of low frequency hearing were also reported as anticipated adverse events.

Changes in low frequency hearing sensitivity at the six month study endpoint are summarized below:

- 33 subjects maintained hearing of a severe degree or better, referred to as functional acoustic hearing
- 17 experienced a decrease in low frequency hearing resulting in profound loss of hearing, referred to as nonfunctional acoustic hearing.

It is difficult to predict on an individual basis what post-operative hearing will be since the causes are likely multi-factorial. Pre- and post-operative hearing sensitivity changes at the six month endpoint are summarized below:

- Of the 14 subjects who began with a low frequency PTA of 40dB or better, 13 subjects had a post-operative low frequency PTA of 90dB or better (92.3%)
- Of the 26 subjects who began with a low frequency PTA of between 41dB and 55dB, 17 subjects had a post-operative low frequency PTA of 90dB or better (65.4%)
- Of the 10 subjects who began with a low frequency PTA of between 56dB and 70dB, 3 subjects had a post-operative low frequency PTA of 90dB or better (30.0%).

For the CNC word test in the implant ear alone condition, 96.0% of subjects performed equal to or better at the six month interval, as compared to pre-operative performance. For the AzBio sentence in noise test in the implant ear alone condition, 89.8% of subject performed equal to or better. No subject, regardless of changes in low frequency hearing, showed a significant decrement in speech perception pre- to post-operatively in the Everyday condition, regardless of the level of post-operative hearing. Averaged across frequencies, the largest drop in thresholds was seen at Initial Activation (four weeks after surgery). Average thresholds at the 3, 6, and 12 month intervals are consistent across time intervals.

As documented in the clinical study results, a percentage of individuals will lose their pre-operative low frequency acoustic hearing as a result of Cochlear Nucleus Hybrid L24 cochlear implant surgery. This known risk is disclosed in the Cochlear Nucleus Hybrid L24 cochlear implant system labeling and is strongly recommended as an integral component of pre-operative surgical and device counseling. Irrespective of the post-operative hearing status, most individuals can still be expected to receive substantial functional and speech recognition benefit in the Everyday condition when compared to pre-operative Bilateral Acoustic Mode.

Performance Based on Post-operative Hearing Sensitivity

Figure 2 plots pre-operative and six month postactivation mean scores for subjects with and without functional post-operative acoustic hearing for the CNC Word Recognition Test. Significant pre- to post-operative improvement was evident in both subpopulations, in both implant ear alone (left graph) and everyday conditions (right graph). In the Everyday condition, performance of subjects with functional acoustic hearing (Severe or Better) was 7 percentage points better when compared to the Implant Ear Alone, with a range of -13 to 46 percentage points. The Everyday condition performance of subjects who had nonfunctional acoustic hearing (Profound) was 28 percentage points better than the Implant Ear Alone condition, with a range of -4 to 64 percentage points. It is important to consider that when making use of the Hybrid cochlear implant in concert with all available acoustic hearing, significant improvement was noted for subjects with and without functional acoustic hearing in the implant ear.

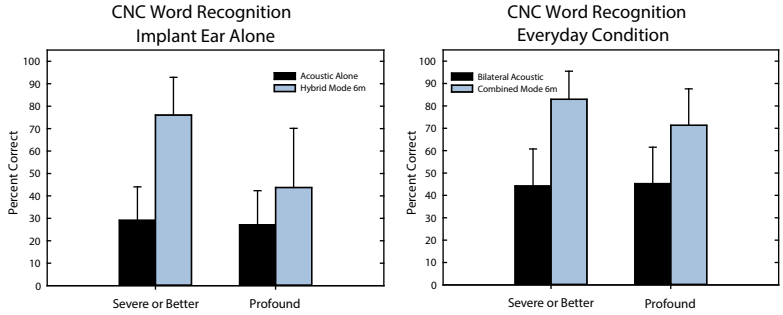

Figure 2: Pre- and 6 month postactivation mean scores for the CNC test for subjects who retained functional acoustic hearing (Severe or Better) and subjects who had nonfunctional acoustic hearing (Profound). The vertical line on each bar represents a +1 Standard Deviation.

Figure 3 plots pre-operative and six month postactivation mean scores for subjects with and without functional post-operative acoustic hearing for the AzBio Sentences in Noise Test. Significant improvement was observed in mean performance for both groups, with the exception of the Implant Ear Alone condition for subjects with nonfunctional acoustic hearing (Profound). In the Everyday condition, performance of subjects with functional acoustic hearing was 7 percentage points better over the Implant Ear Alone, with a range of -11.1 to 42.0 percentage points. The Everyday condition performance of subjects with nonfunctional acoustic hearing was 25 percentage points better than the Implant Ear Alone condition, with a range of -0.4 to 81.5 percentage points. It is important to consider that when making use of the Hybrid cochlear implant in concert with all available acoustic hearing, significant improvement was noted for subjects with and without functional acoustic hearing in the implant ear.

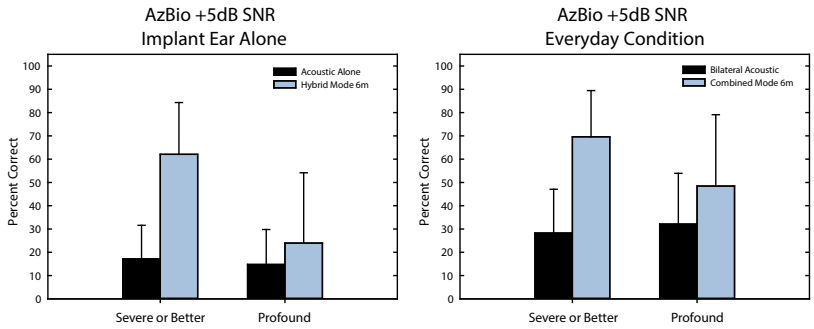

Figure 3: Pre- and 6 month postactivation mean scores for the AzBio test for subjects who retained functional acoustic hearing (Severe or Better) and subjects who had nonfunctional acoustic hearing (Profound). The vertical line on each bar represents a +1 Standard Deviation.

Explantation

Six subjects have been explanted and reimplanted with a conventional cochlear implant. All of these subjects had nonfunctional acoustic hearing and dissatisfaction with post-operative performance, coupled with either no change or a decrease in performance when compared to pre-operative hearing aid performance in the implanted ear. Explantation occurred at 175 days post implantation at the earliest, and 959 days post-implantation at the latest, with an average of 561 days post-implantation.

Each of these subjects underwent a revision surgery with no complications and were implanted with a conventional electrode array. Post-revision reports for four of the subjects indicate improvement in performance as compared to their pre-operative hearing aid condition, as well as prerevision Hybrid outcomes. Their performance is consistent with that seen in standard length CI recipients. Only limited data regarding two subjects' pre- and post-explant performance was available.

Adverse events

The primary safety endpoint was defined as any surgical and/or device-related event, reported as the number and proportion of individuals experiencing the adverse event across the duration of the study. See Table 8 below for a list of Adverse events:

Event	Number of Events	Percentage of Events	Number of Subjects with Event	Percentage of Subjects	Percentage Resolved
Profound Loss	22	31.0%	22	44.0%	0.0%
Open/short circuited electrodes	11	15.5%	11	22.0%	100.0%
Increased tinnitus	6	8.5%	6	12.0%	100.0%
Tinnitus not present pre-operatively	6	8.5%	6	6.0%	100.0%
Explantation/ Reimplantation	6	8.5%	6	12.0%	100.0%
Dizziness	3	4.2%	3	4.0%	100.0%
Dizziness with change in hearing	2	2.8%	2	4.0%	100.0%
Increased tinnitus with change in hearing	2	2.8%	2	4.0%	100.0%
Skin irritation due to externals	2	2.8%	2	4.0%	100.0%
Sound quality issue	2	2.8%	2	4.0%	50.0%
Decrease in performance	1	1.4%	1	2.0%	0.0%
Imbalance	1	1.4%	1	2.0%	100.0%
Imbalance with change in hearing	1	1.4%	1	2.0%	100.0%
Increased impedances with change in hearing	1	1.4%	1	2.0%	100.0%
Local stitch infection	1	1.4%	1	2.0%	100.0%
Overstimulation	1	1.4%	1	2.0%	100.0%
Pain in implant ear	1	1.4%	1	2.0%	100.0%
Vertiginous symptoms with change in hearing	1	1.4%	1	2.0%	100.0%
Vertigo	1	1.4%	1	2.0%	100.0%

Table 8: Number and percentage of adverse events observed for Hybrid L24 subjects

As this study involved implanting subjects with low frequency hearing, unlike prior cochlear implant clinical trials, changes in hearing sensitivity were assessed and those that resulted in profound (> 90 dB HL) loss of low frequency hearing were also reported as anticipated adverse events.

Pre-operative counseling

Prospective cochlear implant candidates should be counseled regarding potential benefits, warnings, precautions and adverse effects of Cochlear Nucleus Hybrid L24 implantation, using the information in this document.

Notes

Notes

Notes





Cochlear™

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Cochlear™

Nucleus® Hybrid™ L24 cochlear implant

CI24REH

Patient Information

Important: Warnings, Precautions and Electromagnetic Compatibility

Hear now. And always

Cochlear®

Symbols

Note

Important information or advice. Can avoid inconvenience.

Caution

Special care to be taken to ensure safety and effectiveness.

Could cause damage to equipment.

Warning (harmful)

Potential safety hazards and serious adverse reactions.

Could cause harm to person.

This document contains important information such as warnings, cautions and privacy that apply to the following cochlear implant systems:

- Cochlear™ Nucleus® Hybrid™ L24 cochlear implant (CI24REH)

Read this document carefully to ensure that you understand the care of your system.

Discuss this information with your physician before undergoing any major medical procedure.

Caution

Federal law restricts this device to sale by or on the order of a physician.

Contents

Glossary

- Everyday Listening Condition – The use of the Cochlear Nucleus Hybrid cochlear implant system in conjunction with a hearing aid in the other ear.
- Cochlear Nucleus Hybrid cochlear implant system – The Cochlear Nucleus Hybrid L24 cochlear implant and Nucleus 6 Sound Processor including coil/cable, battery module, and Remote Assistant, used with or without the acoustic component.
- Implant Ear Alone Condition – The use of the Cochlear Nucleus Hybrid cochlear implant system with no sound input from the other ear or the use of electric hearing with the available low-frequency hearing in the same ear.
- Functional Acoustic Hearing – Acoustic (rather than electric) hearing of a severe degree or better (<90dB).
- Nonfunctional Acoustic Hearing – Acoustic (rather than electric) hearing of a profound degree (≥90dB).

Description of the Cochlear Nucleus Hybrid cochlear implant

A Cochlear Nucleus Hybrid cochlear implant system is designed to bypass damaged parts of the cochlea and allow the auditory nerve to be stimulated. The system consists of a small battery-operated sound processor and microphone, both worn outside the ear, that convert sounds into electrical signals. The signals are transmitted to implant electrodes in the cochlea. The electrodes stimulate the nerve endings in the cochlea so sound can be perceived by the brain.

Cochlear Nucleus Hybrid hearing technology involves the use of an acoustic component in combination with the Cochlear Nucleus Hybrid cochlear implant in the same ear to improve sound perception for patients with challenging hearing losses. The system consists of an in-the-ear (ITE) acoustic module and a cochlear implant sound processor and microphone.

The implant is surgically implanted under the skin behind the ear. It includes a receiver/stimulator to receive and decode the electrical signals and an electrode array to deliver these signals to the cochlea.

The external components include the following sound processors:

- Cochlear Nucleus CP900 series with associated accessories and cables.

Why doctors use the Cochlear Nucleus Hybrid cochlear implant (Indications)

Doctors use the Cochlear Nucleus Hybrid cochlear implant for adults with severe hearing loss in the high pitches (such as birds chirping, children's and women's voices, consonant sounds like 's' and 'sh') but functional hearing in the low pitches. Often people with this hearing loss experience difficulty understanding speech, especially in noisy environments.

The Cochlear Nucleus Hybrid L24 cochlear implant system is intended to provide electric stimulation to the mid- to high-frequency region of the cochlea and acoustic amplification to the low-frequency regions for patients with residual low-frequency hearing sensitivity. The system is indicated for unilateral use in patients aged 18 years and older who have residual low-frequency hearing sensitivity and severe to profound high-frequency sensorineural hearing loss, and who obtain limited benefit from appropriately fitted bilateral hearing aids.

- Typical pre-operative hearing of candidates ranges from normal to moderate hearing loss in the low frequencies (thresholds no poorer than 60 dB HL up to and including 500 Hz), with severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥ 75 dB HL), and moderately severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥ 60 dB HL) in the contralateral ear.
- The CNC word recognition score will be between 10% and 60%, inclusively, in the ear to be implanted in the pre-operative aided condition and in the contralateral ear will be equal to or better than that of the ear to be implanted but not more than 80% correct.

Prospective candidates should go through a suitable hearing aid trial, unless already appropriately fitted with hearing aids.

Who cannot receive the Cochlear Nucleus Hybrid cochlear implant (Contraindications)

A Cochlear Nucleus Hybrid cochlear implant is not indicated for individuals who have the following conditions:

1. Deafness due to lesions of the acoustic nerve or central auditory pathway
2. Active middle ear disease, with or without tympanic membrane perforation
3. Absence of cochlear development
4. A duration of severe to profound hearing loss of 30 years or greater.

⚠ Things you must do to avoid serious harm (Warnings)

Tell your doctor that you have a cochlear implant before undergoing any medical or surgical treatment. Certain types of treatments could injure you or cause damage to your implant. Some of these treatments are listed below

Medical treatments generating induced currents

Below are some medical treatments that generate induced currents which may cause tissue damage or permanent damage to the implant.

Electrosurgery

Electrosurgical instruments are capable of inducing radio frequency currents that could flow through the electrode array. Monopolar electrosurgical instruments must not be used on the head or neck of an implant patient as induced currents could cause damage to cochlear tissues or permanent damage to the implant. Bipolar electrosurgical instruments may be used on the head and neck of patients; however, the cautery electrodes must not contact the implant and should be kept more than 1 cm (~0.5 in.) from the extracochlear electrodes.

Diathermy

Therapeutic or medical diathermy (thermopenetration) using electromagnetic radiation (magnetic induction coils or microwave) should not be used. High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant.

Medical diathermy using ultrasound may be used below the head and neck.

Neurostimulation

Neurostimulation should not be used directly over the implant. High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant.

Electroconvulsive therapy

Electroconvulsive therapy should not be used on an implant patient under any circumstances. Electroconvulsive therapy may cause tissue damage to the cochlea or damage to the implant.

Ionizing radiation therapy

Ionizing radiation therapy should not be used directly over the implant because it may cause damage to the implant.

Magnetic Resonance Imaging (MRI)

MRI is contraindicated for patients with the Cochlear Nucleus Hybrid cochlear implant.

Meningitis

Prior to implantation, candidates should consult their primary care physician and implanting surgeon regarding their vaccination status against organisms that cause meningitis. Meningitis is a known risk of inner ear surgery and candidates for the Cochlear Nucleus Hybrid cochlear implant should be appropriately counseled of this risk.

In addition, certain pre-operative conditions may increase the risk of meningitis with or without an implant. These conditions include:

- Mondini's syndrome and other congenital cochlear malformations
- Concurrent Cerebrospinal Fluid (CSF) shunts or drains
- Recurrent episodes of bacterial meningitis prior to implantation
- Perilymph fistulas and skull fracture/defect with CSF communication.

Long term effects of electrical stimulation

Most patients can benefit from electrical stimulation levels that are considered safe, based on animal experimental data. For some patients, the levels needed to produce the loudest sounds exceed these levels. The long-term effects of such stimulation in humans are unknown. There is no long-term data available on the effects of electrical stimulation on hearing sensitivity.

Head trauma

A blow to the head in the area of the implant may damage the implant and result in its failure. For recommendations on how to minimize the chance of experiencing head trauma see http://www.cdc.gov/ncipc/pub-res/tbi_toolkit/patients/preventing.htm

External sound processor warnings

Rechargeable batteries

In certain circumstances, rechargeable batteries can become VERY HOT, and could cause injury. Remove your processor immediately if it becomes unusually warm or hot, and seek advice from your clinician. Caregivers should touch the recipient's processor to check for heat if the recipient is showing signs of discomfort. Rechargeable batteries should NEVER be worn beneath clothing (including scarves and headwear covering the ears). The rechargeable battery should not be used by patients who cannot remove the device by themselves, or notify a caregiver that the device has become hot.

Overheating of external devices

Remove your processor immediately if it becomes unusually warm or hot, and seek advice from your clinician. Caregivers should touch their recipient's processor to check for heat if the recipient is showing signs of discomfort.

The manufacturer only recommends the use of Cochlear rechargeable battery modules and zinc air disposable batteries.

The processor is not intended to be used with silver oxide batteries. In some circumstances, the use of these batteries could result in severe burns. A dangerous amount of heat can be generated by these batteries in conditions where heat cannot dissipate, especially if the device is being held against the skin by clothing or a retention device. In addition, use of silver oxide batteries may damage your processor.

⚠ Things you must do to avoid other harm (Precautions)

Use the implant system only with the approved devices and accessories listed in the user guide.

Your processor and other parts of the system contain complex electronic parts. These parts are durable but must be treated with care. The opening of your processor by anyone other than Cochlear's qualified service personnel invalidates the warranty.

If you experience a significant change in performance or the sound becomes uncomfortable, turn off your processor and contact your implant center.

Each processor is programmed specifically for each implant. Never wear another person's processor or lend yours to another user.

Using the wrong processor could result in loud or distorted sounds that, in some instances, may cause extreme discomfort.

Do not operate your processor at temperatures above +40 °C (+104 °F) or less than +5 °C (+41 °F).

Do not store your processor at temperatures above +50 °C (+122 °F) or less than -20 °C (-4 °F).

Your processor's sound quality may be intermittently distorted when you are within approximately 1.6 km or 1 mile of a radio or television transmission tower. Additional sources of interference include, but are not limited to:

- Security systems
- Industrial machinery and power systems
- Mobile communications equipment (including cellular telephones and certain kinds of hand-held, two-way radios (including Citizen Band, Family Radio Service, and Amateur Band).

To reduce or eliminate the interference, move away from the source. If your processor stops working, turn the power switch off and then back on. This effect is temporary and will not damage your processor.

Small parts hazard

Caregivers should be counseled that the external sound processor contains small parts that may be hazardous if swallowed or may cause choking if ingested or inhaled.

Use of batteries and battery ingestion

When using disposable batteries with the sound processor, only use battery types recommended by your clinician or Cochlear. Other types may not have sufficient energy to allow your processor to operate for a long time.

Cochlear does not recommend the use of silver oxide or alkaline batteries.

Batteries can be harmful if swallowed. Ensure that batteries are kept out of reach of young children. If swallowed, seek prompt medical attention at the nearest emergency center.

Theft and metal detection systems

Devices such as airport metal detectors and commercial theft detection systems produce strong electromagnetic fields. Some implant recipients may experience a distorted sound sensation when passing through or near one of these devices. To avoid this, turn off your processor when in the vicinity of one of these devices.

The materials used in the implant may activate metal detection systems. For this reason, recipients should carry the Cochlear Implant Patient Identification Card with them at all times.

Electrostatic discharge

A discharge of static electricity can damage the electrical components of the implant system or corrupt the program in your processor.

If static electricity is present (e.g. when putting on or removing clothes over the head, or getting out of a vehicle), implant recipients should touch something conductive (e.g. a metal door handle) before the implant system contacts any object or person.

Prior to engaging in activities that create extreme electrostatic discharge, such as playing on plastic slides, the processor should be removed.

Mobile telephones

Some types of digital mobile telephones (e.g. Global System for Mobile communications (GSM) as used in some countries) may interfere with the operation of the external equipment. As a result, implant recipients may perceive a distorted sound sensation when in close proximity, 1–4 m (~3–12 ft), to a digital mobile telephone in use.

Scuba diving

Implant Type	Maximum depth
CI24REH Implant	40m (~131 ft)

Table 1: Maximum diving depths when wearing implants

The Sound Processor must be removed before diving. Recipients should seek medical advice before participating in a dive for conditions that might make diving contraindicated, for example middle ear infection, etc. When wearing a mask, avoid pressure over the implant site.

Sleeping

Do not wear your processor while sleeping, as you may not become aware of your processor becoming unusually warm or hot.

Retention aids

When using retention aids such as the Snugfit™ or LiteWear, be aware that it may take longer to remove the processor if the processor becomes unusually warm or hot.

Do not attach the LiteWear beneath layers of clothing.

Electromagnetic interference with medical devices

Cochlear Nucleus Remote Assistants meet defined international Electromagnetic Compatibility (EMC) and emission standards. However, because the remote assistant radiates electromagnetic energy, it is possible that it could interfere with other medical devices such as cardiac pacemakers and implantable defibrillators when used nearby. It is recommended that the Remote Assistant is kept at least 6 in. (~15.2 cm) away from devices which could be subject to electromagnetic interference. For added assurance, please also consult the recommendations provided by the device manufacturer.

Electromagnetic Compatibility (EMC)

Guidance and manufacturer's declaration

The Cochlear Nucleus Series Sound Processor and Remote Assistant are intended for use in the electromagnetic environments specified in this document.

They have been tested and found to be in compliance as shown. You should take care to use your processor as described.

Electromagnetic emissions

Emission test	Compliance	Guidance
RF emissions CISPR 11	Group 1	RF energy is only used for its internal function. The RF emissions are very low and not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The device is suitable for use in all establishments, including domestic establishments and those directly connected to public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable	
Voltage fluctuations/flicker emissions IEC 61000-3-3		

Table 2: Electromagnetic emissions

Electromagnetic immunity

Immunity test	IEC 60601 test level	Compliance level	Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±6 kV contact ±8 kV air	±6 kV contact ±8 kV air	See *Electrostatic discharge* on page 16
Electrical fast transient/burst IEC 61000-4-4	Not applicable		
Surge IEC 61000-4-5			
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11			
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields be at levels characteristic of a typical location in a typical commercial or hospital environment
Conducted RF IEC 61000-4-6 Radiated RF IEC 61000-4-3	Not applicable 3 V/m 80 MHz to 2.5 GHz	3 V/m	See the *Warnings* and *Precautions* sections, and *Guidance* below

Table 3: Electromagnetic immunity

Guidance

Portable and mobile RF communications equipment should be used no closer to any part of the devices, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.

Recommended separation distance (d):

$d = 1.2\sqrt{P}$ 80 MHz to 800 MHz

$d = 2.3\sqrt{P}$ 800 MHz to 2.5 GHz

where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in metres (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.[b]

Interference may occur in the vicinity of equipment marked with the following symbol:

Note

1. At 80 MHz and 800 MHz, the higher frequency range applies.
2. These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Explanatory notes:

a. Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the processor is used exceeds the applicable RF compliance level above, the processor should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the processor.

b. Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

Recommended separation distances

Your processor is intended for use in an electromagnetic environment where the radiated RF disturbances are controlled.

To prevent electromagnetic interference, maintain a minimum distance between the portable and mobile RF communications equipment (transmitters) and the device as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (W)	Separation distance according to frequency of transmitter (m)		
	150 kHz to 80 MHz $d = 1.2\sqrt{P}$	80 MHz to 800 MHz $d = 1.2\sqrt{P}$	800 MHz to 2.5 GHz $d = 2.3\sqrt{P}$
0.01	Not applicable	0.12	0.23
0.1		0.38	0.73
1		1.2	2.3
10		3.8	7.3
100		12	23

Table 4: Recommended separation distances

For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

Note

1. At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.
2. These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Risks of receiving the Cochlear Nucleus Hybrid cochlear implant

Certain risks are a part of all surgery. Candidates should discuss the known risks, benefits and alternatives to Cochlear Nucleus Hybrid hearing technology with their surgeon and audiologist. The following are known limitations associated with cochlear implantation, which may also apply to the Cochlear Nucleus Hybrid cochlear implant:

- Speech and other sounds will not sound the same as they would for a normal-hearing person, though most patients accommodate to the sound in a relatively short period of time.
- Some participants may not have sufficient auditory nerve fibers to allow successful electrical stimulation.
- For some participants, the Cochlear Nucleus Hybrid cochlear implant may not provide useful speech understanding.

The loss of residual hearing is a risk of receiving the Cochlear Nucleus Hybrid cochlear implant. In a clinical study, at six months post-implant most individuals (90%) retain a level of acoustic hearing and many (66%) utilize that hearing with or without amplification at the implant ear. For some individuals (34% in this study), a profound loss of functional acoustic hearing in the implanted ear may occur.

Changes in low frequency hearing sensitivity six months after surgery are summarized below:

- 33 subjects maintained hearing of a severe degree or better, called functional acoustic hearing
- 17 experienced a decrease in low frequency hearing resulting in profound loss of hearing, called nonfunctional acoustic hearing.

Six months after implantation, the average change in low frequency hearing was 33 dB.

Five more subjects experienced a decrease in low frequency hearing resulting in profound loss of hearing after six months, this happened between one and four years after surgery.

Speech performance data is listed below. This data includes subjects who had both functional and nonfunctional acoustic hearing.

Word Recognition Test

- Average performance after six months of experience using the device, in the Implant Ear Alone condition:
  - For subjects with functional acoustic hearing, scores increased from 29.1% to 76.0%
  - For subjects with nonfunctional acoustic hearing, scores increased from 26.7% to 43.7%.
- Average performance after six months of experience using the device, in the Everyday condition:
  - For subjects with functional acoustic hearing, scores increased from 44.2% to 82.9%
  - For subjects with nonfunctional acoustic hearing, scores increased from 45.3% to 71.3%.

As shown above, both subject groups showed significant improvement with and without functional acoustic hearing. This was true in both Implant Ear Alone and Everyday conditions. The addition of the opposite (not implanted) ear showed further benefit. Moving from the Implant Ear Alone to the Everyday condition further increased performance. For subjects with functional acoustic hearing, this increase was 7 percentage points. The range of this change was -13 to 46 percentage points. For subjects with nonfunctional acoustic hearing, this increase was 28 percentage points. The range of this change was -4 to 64 percentage points. When using the Cochlear Nucleus Hybrid cochlear implant along with all acoustic hearing, significant improvement was noted. This was true for subjects both functional and nonfunctional acoustic hearing.

Sentence Recognition in Noise Test

- Average performance after six months of experience using the device, in the Implant Ear Alone condition:
  - For subjects with functional acoustic hearing, scores increased from 17.2% to 62.1%
  - For subjects with nonfunctional acoustic hearing, scores increased from 15.4% to 23.9%.
- Average performance after six months of experience using the device, in the Everyday condition:
  - For subjects with functional acoustic hearing, scores increased from 28.3% to 69.5%
  - For subjects with nonfunctional acoustic hearing, scores increased from 32.1% 48.4%.

As shown above, both subject groups showed significant improvement with and without functional acoustic hearing. This was true in both Implant Ear Alone and Everyday conditions, with one exception. There was no significant difference for subjects with nonfunctional acoustic hearing in the Implant Ear Alone condition. The addition of the opposite (not implanted) ear showed further benefit. Moving from the Implant Ear Alone to the Everyday condition further increased performance. For subjects with functional acoustic hearing, this increase was 7 percentage points. The range of this change was -11.1 to 42.0 percentage points. For subjects with nonfunctional acoustic hearing, this increase was 25 percentage points. The range of this change was -0.4 to 81.5 percentage points. When using the Cochlear Nucleus Hybrid cochlear implant along with all acoustic hearing, significant improvement was noted. This was true for subjects both functional and nonfunctional acoustic hearing.

For the CNC and AzBio tests in the implant ear alone, 96.0% and 89.8% of subjects performed equal to or better at six months as compared to pre-operative scores. It is important to note that no subject, regardless of post-operative acoustic hearing, showed a decrease in the Everyday condition. Averaged across frequencies, the largest improvement in thresholds was seen at Initial Activation (4 weeks after surgery). Average thresholds at the 3, 6, and 12 month intervals are consistent across time intervals.

Below is a table that summarizes the most frequent hazards associated with implant surgery in the Cochlear Nucleus Hybrid Clinical Trial. The events that occurred were anticipated and are reflective of those found in otologic procedures.

- Items in the 'Hazard' column are the things that happened because of the use of the Cochlear Nucleus Hybrid cochlear implant
- Items in the 'How often patient had the hazard' column are the frequencies that were observed for the 'Hazard'
- Items in the 'Harm' column are the results of the 'Hazard' that were observed
- Items in the 'How often this hazard harmed them' column are the frequencies at which the 'Harm' happened for this 'Hazard'.

Event: Implantation with Cochlear Nucleus Hybrid cochlear implant			
Hazard	How often patient had the hazard	Harm	How often this hazard harmed them
Tinnitus	14 out of 50 patients	Tinnitus that did not resolve or change in hearing	0 of these 14 patients had tinnitus that did not resolve, 2 out of these 14 patients had a change in hearing
Dizziness (Imbalance/ Vertigo)	9 out of 50 patients	Dizziness, imbalance, or vertigo that did not resolve or a change in hearing	0 of these 9 patients had dizziness (imbalance/vertigo) that did not resolve, 4 of these 9 patients had a change in hearing
Profound loss of hearing	22 out of 50 patients	No recovery	22 out of these 22 patients
Electrode malfunction	11 out of 50 patients	Possible performance decrement	0 of these 11 patients

Event: Implantation with Cochlear Nucleus Hybrid cochlear implant			
Hazard	How often patient had the hazard	Harm	How often this hazard harmed them
Explantation/ Reimplantation	6 out of 50 patients	Additional surgery due to hearing loss	6 of the 6 patients
Skin irritation	2 out of 50 patients	Discomfort	0 of these 2 patients
Sound quality issue	2 out of 50 patients	Long term sound quality issue	1 of these 2 patients
Decrease in performance	1 out of 50 patients	Long term decreased performance	1 of the 1 patients
Increased impedances with change in hearing	1 out of 50 patients	Change in hearing	0 of the 1 patient
Local stitch infection	1 out of 50 patients	Discomfort, use of antibiotics	1 of the 1 patient
Overstimulation	1 out of 50 patients	Discomfort that did not resolve	0 of the 1 patient
Pain in implant ear	1 out of 50 patients	Discomfort that did not resolve	0 of the 1 patient

Table 5: Most frequent hazards from Cochlear Nucleus Hybrid Clinical Trial

Explantation

As part of the study, six subjects had surgery to remove their Cochlear Nucleus Hybrid cochlear implant and replace it with a typical cochlear implant. All of these subjects had no functional acoustic hearing in the implanted ear, and were dissatisfied with their performance. This was coupled with either a decrease or no change in the performance of the implanted ear. The earliest explantation occurred after 175 days, and the latest after 959 days. The average time before explanation for these subjects was 561 days.

No subjects had complications with revision surgery. Data gathered after the reimplantation for four of the subjects shows performance improvement. This is true when compared to performance both before the initial surgery and before the revision. After being reimplanted, the subjects' performance was similar to performance of conventional cochlear implant recipients. Limited data was available for two of the subjects.

Benefits of receiving the Cochlear Nucleus Hybrid cochlear implant

The potential benefits of the Cochlear Nucleus Hybrid cochlear implant for recipients relate to improvements in:

- Better understand speech in both quiet and noisy environments
- Increased satisfaction based on hearing capabilities.

The Cochlear Nucleus Hybrid Clinical Trial showed that recipients on average improved their hearing performance by doubling their hearing performance in quiet and in noise.

80% (40/50) of recipients scored significantly better on word understanding in the implant ear than they could hear with a hearing aid alone in that ear.

100% (50/50) of subjects score same or better in quiet and noise when using the implant in one ear and a hearing aid in the other ear than with hearing aids alone.

Further detail on the benefits of the Cochlear Nucleus Hybrid cochlear implant is provided in the ***How we studied the Cochlear Nucleus Hybrid cochlear implant*** section of this booklet.

How to decide whether to get the Cochlear Nucleus Hybrid cochlear implant

Candidates for the Cochlear Nucleus Hybrid cochlear implant should discuss the known risks, benefits and alternatives to Cochlear Nucleus Hybrid hearing technology with their surgeon and audiologist prior to deciding whether to proceed with implantation.

Before implantation of the Cochlear Nucleus Hybrid cochlear implant

To decide if you are a candidate for the Cochlear Nucleus Hybrid cochlear Implant, your hearing healthcare professional will perform a hearing test. They will also test your speech understanding while using your hearing aids to determine if you meet the criteria for a Cochlear Nucleus Hybrid cochlear implant.

During implantation of the Cochlear Nucleus Hybrid cochlear implant

During implant surgery, the surgeon makes an incision behind the ear, creates a pocket in the bone to house the implant's receiver-stimulator, and threads the electrode array into the cochlea. The post-operative hospital stay is variable and will be determined by the surgeon.

Using the Cochlear Nucleus Hybrid cochlear implant after surgery

An external sound processor is required in order for stimulation of the Cochlear Nucleus Hybrid cochlear implant to occur. Following a healing period of approximately four weeks, the participant will return to the audiologist for initial programming. During this appointment, the audiologist will activate and program the Cochlear Nucleus Hybrid cochlear implant system. The recipient will also be instructed on the use and care of the sound processor.

Please refer to the Sound Processor and Remote Assistant User Manuals for instructions on the operation, care and maintenance of the external components.

Travel

Transmitting devices such as mobile/cell phones sometimes need to be switched off on aircraft. If you have a remote control (Remote Assistant) for your processor, it might also need to be switched off because it is transmitting high frequency radio waves when switched on. You should check with your airline for more information about whether or not you can use your remote. You can wear your sound processor.

How we studied the Cochlear Nucleus Hybrid cochlear implant

A clinical trial was performed to test whether the Cochlear Nucleus Hybrid cochlear implant system was safe and effective for use. Subjects who were part of the study had sensorineural hearing loss. This is usually caused by damage to the hair cells of the cochlea. Subjects also had a specific profile of hearing ability. Subjects had normal hearing to moderate hearing loss in the low frequencies, with severe to profound hearing loss in the high frequencies. Subjects were also tested both with and without a hearing aid in the opposite (not implanted) ear.

When testing the implant ear alone, subjects used the signals from the implant as well as whatever acoustic hearing they kept in the same ear. In everyday life, most patients used a hearing aid in the opposite (not implanted) ear. Because of this, speech understanding abilities were also tested with both ears. This was called the Everyday listening condition.

The study also measured how well subjects could hear at different frequencies. This was tested over time, to measure any changes in hearing. This data was then used to understand what effect being implanted had on the remaining hearing in low frequencies.

Subject Characteristics

Key characteristics of the subjects in the study are shown in Table 6 below.

Demographic characteristics	Mean (min, max)
Age at CI in Years	64.1 (23.0 – 86.2)
Duration of Overall Hearing Loss in Years	28.1 (3.4 – 73.9)
Duration of High Frequency Hearing Loss in Years	13.1 (1.6 – 30.1*)
Male	25/50 (50.0%)
Female	25/50 (50.0%)
Pre-operative Degree of LF PTA (Implanted Ear):	
Normal (0 – 25 dB HL)	1/50 (2.0%)
Mild (26 - 40 dB HL)	13/50 (26.0%)
Moderate (41 – 55 dB HL)	26/50 (52.0%)
Moderate-Severe (56 – 70 dB HL)	10/50 (20.0%)

* One subject met the requirement of < 30 years duration of severe to profound high frequency loss at candidacy assessment but was slightly over 30 years duration by the time surgery was approved for reimbursement and completed.

Table 6: Demographics for the 50 study subjects

Fifty subjects were enrolled in the study and implanted. Forty nine of these completed the six month testing. One subject was explanted before the six month testing. This occurred after poor performance and loss of hearing sensitivity. Of these forty-nine subjects, two only completed speech testing and the SSQ. One subject only completed speech testing. This was due to limits on time and the choice of the clinicians.

Description of Tests

CNC Monosyllabic Word Recognition Test (Primary endpoint)

The CNC Monosyllabic Word Recognition Test was a primary endpoint. This means it was one of the main tests used to judge whether the implant was a success or a failure. The test is made up of 10 recorded lists of 50 words, each with one syllable. Each of these words is made up of a consonant, a nucleus, and a second consonant, such as 'laud' or 'duck'. Two lists are given in quiet conditions, at a volume of 60dBA. The scores are reported as percent of words correct, and percent of phonemes correct.

AzBio Sentence Test (Primary endpoint)

The AzBio Sentence Test was the second primary endpoint. This test is made up of 33 possible lists of 20 sentences. Sentences are meant to have low contextual information, such as 'He cried when the pet goat was sent to market'. Each list includes 5 sentences, from 4 possible different speakers (2 male, 2 female). Two lists of the AzBio sentences are presented at a volume of 60 dBA. These sentences are presented with competing noise in the form of multiple people talking, or 'babble'. The sentences are presented 5dB louder than the competing noise, from the same loudspeaker.

University of Washington Clinical Assessment of Music Perception (UW-CAMP)

The UW-CAMP test is made up of three subtests. Each are made to test different auditory skills which are important for hearing music. The three subtests were presented at 65 dBA, and tested pitch perception, melody recognition, and timbre.

The Speech, Spatial, and Qualities of Sound Questionnaire (SSQ)

The SSQ is a validated self-assessment metric commonly used in hearing aid and cochlear implant research. It is designed to measure self-reported auditory disability across a wide variety of domains, reflecting the reality of hearing in the everyday world. There are 49 questions scored by the subject using a scale of 0 through 10, where 0 corresponded to minimal ability and 10 corresponded to complete ability. There are three specific hearing domains assessed:

The SSQ is a validated self-assessment widely used in hearing research. It is made to test the extent of hearing disability in a variety of situations. This way, it can capture the reality of hearing in the everyday world. There are 49 questions scored by the subject on a scale of 0 to 10. 0 corresponds to minimal ability, and 10 corresponds to complete ability. There are three different areas that are tested:

- Speech hearing scale – This includes hearing speech in quiet and in noise, in one-on-one conversation and in groups/meetings.
- Spatial hearing scale – This includes hearing where sounds are coming from, distance, movement, and ability to segregate sounds.
- Qualities of sound scale – This includes ease of listening, naturalness, clarity, identification of different speakers, musical pieces and instruments, as well as everyday sounds.

Device Use Questionnaire (DUQ)

The DUQ was created by Cochlear to collect information from patients directly. Specifically, the questionnaire asks about ease and satisfaction with the device in different environments and situations. The questionnaire is about 90 items long. The questions that appear in this bulletin are related to satisfaction. Other questions related to the ways the subjects used the device—these are left out for brevity.

Speech perception

Forty-nine of fifty subjects had speech perception data at the six month interval.

Understanding Speech in Quiet – CNC Monosyllabic Word Test

Everyday Listening condition

- Average performance after six months was significantly higher than average performance using two hearing aids prior to implantation
  - Average CNC scores were 44.9% (2% - 81%) pre-operatively with two hearing aids and 79.4% (35% - 98%) at six months post-operative in the Everyday listening condition
- After six months of post-operative experience:
  - All subjects (49/49; 100%) demonstrated similar or better word recognition (CNC) compared with their pre-operative performance using two hearing aids
  - Most (43/49; 87.8%) demonstrated significantly better word recognition compared with their pre-operative performance using two hearing aids.

Implant Ear Alone condition

- Average performance after six months was significantly higher than average performance for the subjects using one hearing aid prior to implantation
  - Average CNC scores were 28.4% (9% - 64%) pre-operatively with one hearing aid and 65.4% (8% - 98%) at six months in the Implant Ear Alone condition.
- After six months of post-operative experience:
  - Most subjects (47/49; 96%) demonstrated similar or better word recognition (CNC) compared with their pre-operative performance using one hearing aid
  - Most (40/49; 81.6%) demonstrated significantly better word recognition compared with their pre-operative performance using one hearing aid.

Understanding Speech in Noise – AzBio Sentence Test in Noise (+5 dB SNR)

Everyday Listening Condition

- Average performance after six months was significantly higher than average performance for the subjects using two hearing aids prior to implantation
  - Average AzBio sentences in noise scores were 29.6% (0.0% - 76.5%) pre-operatively with two hearing aids and 62.6% (3.6% - 92.7%) at six months in the Everyday listening condition.

- After six months of post-operative experience:
  - Most recipients (49/49; 100%) demonstrated similar or better sentence recognition in noise (AzBio) compared with their pre-operative performance using two hearing aids
  - Most (41/49; 84%) demonstrated significantly better sentence recognition in noise (AzBio) compared with their pre-operative performance using two hearing aids.

Implant Ear Alone Condition

- Average performance after six months was significantly higher than average performance for the subjects using one hearing aid prior to implantation
  - Average AzBio sentences in noise scores were 16.3% (0.0% - 64.1%) pre-operatively with one hearing aid and 49.2% (0.0% - 91.5%) at six months in the Implant Ear Alone Condition.
- After six months of post-operative experience:
  - Most subjects (44/49; 89.8%) demonstrated similar or better sentence recognition in noise (AzBio) compared with their pre-operative performance using one hearing aid
  - Many (36/49; 73.5%) demonstrated significantly better sentence recognition in noise (AzBio) compared with their pre-operative performance using one hearing aid.

80% (40/50) of recipients scored significantly better on word understanding in the implant ear than with a hearing aid alone.

100% (50/50) of subjects score same or better in quiet and noise when using the Cochlear Nucleus Hybrid cochlear implant in one ear and a hearing aid in the other ear than with hearing aids alone.

Music Performance – University of Washington Clinical Assessment of Music Perception (UW-CAMP)

Forty-six of fifty subjects had music performance scores available at the six month interval.

Everyday Listening Condition

Pitch Discrimination

- Post-operative average pitch discrimination ability was similar to that observed for normally hearing individuals1
- Performance was unchanged pre-operatively with two hearing aids to post-operatively at six months
  - Average pitch discrimination was 1.1 (0.5 – 6.3) semitones pre-operatively compared to 1.1 (0.5 – 3.7) semitones at six months.
- After six months of post-operative experience:
  - Most recipients (41/47; 87.2%) demonstrated similar (within 1 semitone) or better pitch discrimination compared with their pre-operative performance using two hearing aids.

Implant Ear Alone Condition

Pitch Discrimination

- Average performance remained relatively unchanged pre-operatively with one hearing aid to post-operatively at six months:
  - Average pitch discrimination was 1.1 (0.5 – 4.8) semitones pre-operatively compared to 1.5 (0.5 – 8.9) semitones at six months.
- After six months of experience:
  - Most recipients (42/46; 91.3%) demonstrated similar (within 1 semitone) or better pitch discrimination compared with their pre-operative performance using one hearing aid.

Device Use Questionnaire – Music

- When compared to pre-operative levels, satisfaction improved across all six music/sound quality related areas at the six month post-operative interval
  - When listening to live music with singing, satisfaction increased from 8.5% to 53.3%
  - When listening to live music without singing, satisfaction increased from 42.6% to 62.2%
  - When listening to recorded music with singing, satisfaction increased from 6.0% to 57.4%
  - When listening to recorded music without singing, satisfaction increased from 28.6% to 66.0%
  - When listening to music in general, satisfaction increased from 26.0% to 58.3%.

Self-assessment

Speech, Spatial, and Qualities of Hearing (SSQ) Scale – based on the Everyday Listening condition

Forty-eight of fifty subjects had SSQ ratings available at the six month interval. This data was divided into three sub-scales: Speech Hearing, Spatial Hearing and Sound Qualities. For all three scales, the subject rated their ability to hear. Ratings were on a scale from 1 to 10, where 1 was the poorest rating possible and 10 was the best rating possible. All subscales applied were applied to two hearing aids pre-operatively. After implantation, the subscales were applied to the Everyday condition.

Speech Hearing Rating Scale

The Speech Hearing Scale addressed how well subjects could hear and understand speech in various quiet and noisy situations. These included one-on-one conversations and speech in small and large groups of people.

- Average performance after six months was significantly higher than performance prior to implantation
  - Pre-operatively, average ratings were 3.2 (0.8 – 6.2) out of 10 compared to 5.4 (0.7 – 8.8) out of 10 at six months.
- After six months of experience:
  - Most recipients (45/48; 93.8%) demonstrated similar or better ratings for the Speech Hearing Scale compared with their pre-operative performance
  - Most (37/48; 77.1%) reported benefit to very high benefit on the Speech Hearing Scale compared with their pre-operative performance.

Spatial Hearing Rating Scale

The Spatial Hearing Scale addressed how well subjects could judge directionality of sound. This included where a sound was coming from, how far away the sound was, and movement of sound (e.g., whether a sound was coming toward them or away from them).

- Average performance after six months was significantly higher than average performance prior to implantation for the Spatial Hearing Scale
  - Pre-operatively, average ratings were 4.6 (1.4 – 9.2) out of 10 compared to 5.5 (1.1 – 8.3) out of 10 at six months.
- After six months of experience:
  - Most recipients (39/48; 81.3%) demonstrated similar or better ratings for the Spatial Hearing Scale compared with their pre-operative performance
  - Many (26/48; 54.2%) reported benefit to very high benefit on the Spatial Hearing Scale compared with their pre-operative performance.

Sound Qualities Rating Scale

The Sound Qualities Scale addressed how well subjects could separate and sort out sounds and how well they could recognize different sounds. It also addressed how clear or natural sounds were, and how much effort listening required.

- Average performance after six months was significantly higher than average performance prior to implantation for the Spatial Hearing Scale
  - Pre-operatively, average ratings were 5.0 (1.6 – 8.1) out of 10 with two hearing aids and 6.3 (2.7 – 9.1) out of 10 at six months
- After six months of experience using the Everyday listening condition:
  - Most recipients (43/48; 89.6%) demonstrated similar or better ratings for the Sound Qualities Scale compared with their pre-operative performance
  - Many (28/48; 58.3%) reported benefit to very high benefit on the Sound Qualities Scale compared with their pre-operative performance.

Device Use Questionnaire

- When compared to pre-operative levels, overall satisfaction increased at the six month interval
  - The number of subjects satisfied with their performance increased from 8.0% to 79.2%
- When compared to pre-operative levels, satisfaction improved across all seven listening situations at the six month interval
  - When listening using a telephone, satisfaction increased from 10.0% to 29.2%
  - When listening in a noisy environment, satisfaction increased from 0.0% to 33.3%
  - When listening in a quiet environment, satisfaction increased from 34.0% to 85.4%
  - When listening in a one-on-one situation, satisfaction increased from 44.0% to 93.8%
  - When listening in a small group situation, satisfaction increased from 16.0% to 75.0%
  - When listening in a large group situation, satisfaction increased from 2.0% to 45.8%
  - When listening to a source at a distance (in church, at a music hall), satisfaction increased from 6.0% to 50.0%
  - When listening to the outdoors (birds, nature sounds, etc.), satisfaction increased from 32.7% to 83.0%.

Where you can find more information

For additional information concerning Cochlear Americas and the Cochlear Nucleus Hybrid cochlear implant, visit Cochlear's website at www.cochlear.com or call 1 800 523 5798.

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