DEPARTMENT OF HEALTH & HUMAN SERVICES

POS file

Public Health Service

Memorandum

P940022

Date MAR 22 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Advanced Bionics™ Corporation
CLARION™ Multi-Strategy Cochlear Implant - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Jane Fredericksen, CDRH, 1/30/96, 594-2080
Marilyn Flack, CDRH, 1/30/96, 594-2080
Harry Sauberman, CDRH, 1/30/96, 594-2080
David Segerson, CDRH, 1/30/96, 594-2080

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

DRAFT

Food and Drug Administration

DOCKET NO.

Advanced Bionics Corp.; Premarket Approval of Clarion Multi-Strategy Cochlear Implant

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the Premarket Approval Application by Advanced Bionics Corp., Sylmar, CA 91342, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Clarion Multi-Strategy Cochlear Implant. After reviewing the recommendation of the Ear, Nose and Throat Devices Advisory Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on March 22, 1996, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER);

ADDRESSES: Address written requests for copies of the summary of safety and effectiveness data, and petitions for administrative review to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

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FOR FURTHER INFORMATION CONTACT:

Jane Fredericksen,

Center for Devices and Radiological Health (HFZ-470),

Food and Drug Administration,

9200 Corporate Blvd.,

Rockville, MD 20850,

301-594-2080.

SUPPLEMENTARY INFORMATION: On June 30, 1994, Advanced Bionics Corp., Sylmar, CA 91342, submitted to CDRH an application for premarket approval of the Clarion Multi-Strategy Cochlear Implant. The Clarion Multi-Strategy Cochlear Implant is intended to restore a level of auditory sensation to individuals with profound sensorineural deafness via electrical stimulation of the auditory nerve. Clarion is indicated for use in postlingually deafened adults, 18 years of age or older, with profound, bilateral, sensorineural deafness (greater than or equal to 90 dBHL), who are unable to benefit from appropriately fitted hearing aids. Lack of aided benefit from a hearing aid is defined as scoring 20% or less on tests of open-set sentence recognition (i.e., CID Sentences). Additionally, there should be no radiographic contraindications to receiver placement or electrode insertion.

On July 21, 1995, the Ear, Nose and Throat Devices Advisory Panel, an FDA advisory panel, reviewed and recommended conditional approval of the application.

On March 22, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this supplemental application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and regulations or a review of the supplemental application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Dorcas K. Kessler
Director, Clinical Research
and Regulatory Affairs
Advanced Bionics Corporation
12740 San Fernando Road
Sylmar, California 91342

MAR 22 1996

Re: P940022
Clarion Multi-Strategy Cochlear Implant
Filed: June 30, 1994
Amended: September 23, 1994, November 9, 1994, December 5, 1994, December 13, 1994, January 23, 1995, January 31, 1995, March 13, 1995, June 20, 1995, June 21, 1995, June 22, 1995, July 6, 1995, July 14, 1995, July 19, 1995, July 28, 1995, July 31, 1995, September 28, 1995, October 5, 1995, October 25, 1995, November 21, 1995, December 22, 1995, December 26, 1995, December 27, 1995, February 7, 1996 and February 14, 1996

Dear Ms. Kessler:

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 Clarion Multi-Strategy Cochlear Implant for use in an adult population. The Clarion Multi-Strategy Cochlear Implant is intended to restore a level of auditory sensation to individuals with profound sensorineural deafness via electrical stimulation of the auditory nerve. Clarion is indicated for use in postlingually deafened adults, 18 years of age or older, with profound, bilateral sensorineural deafness (greater than or equal to 90 dBHL), who are unable to benefit from appropriately fitted hearing aids. Lack of aided benefit is defined as scoring 20% or less on tests of open-set sentence recognition (CID Sentences).

The PMA application is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may

begin commercial distribution of the device upon receipt of this letter contingent upon the conditions cited on page 3.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the postmarket study data and statistical analysis described below. This postmarket study is designed to monitor the long-term safety and effectiveness of the Clarion Multi-Strategy Cochlear Implant. The study must include the following:

> Data from the 66 patients implanted at 7 of the 29 investigational sites should be provided. These 7 sites are identified in Amendment 23, dated December 21, 1995. In addition, data should be provided from patients implanted at the other 22 investigational sites who are presently utilizing the Compressed Analog (CA) strategy and/or bipolar stimulation (either CA or Continuous Interleaved Strategy (CIS)).
>
> The patients included in the postapproval study must be followed for a period of 5 years from date of implantation.

The postmarket study must include the following evaluations:

1. statistical trend analyses of electrode impedance, electrical thresholds, and electrical dynamic range;

2. medical/surgical complications;

3. device failure reports;

4. trend analyses of safety parameters for patients using

bipolar stimulation with either CA or CIS processing strategies, and for patients using monopolar CA ; and

5. scores of CID Sentences and HINT Sentences for all patients considered in the postmarket study.

Expiration dating for this device has been established and approved at two years.

CDRH will publish a notice of its decision to approve your PMA application in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

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

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Jane Fredericksen at (301) 594-2080.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Cochlear Implant

Device Trade Name: CLARION™ Multi-Strategy™ Cochlear Implant System

Applicant's Name
and Address: Advanced Bionics™ Corporation
12740 San Fernando Road
Sylmar, California 91342

Premarket Approval Application (PMA) Number: P940022

Date of Panel Recommendation: July 21, 1995

Date of Notice of Approval to the Applicant: MAR 2 2 1996

II. INDICATIONS FOR USE

The CLARION™ Multi-Strategy Cochlear Implant, hereinafter referred to as CLARION, is intended to restore a level of auditory sensation to individuals with profound sensorineural deafness via electrical stimulation of the auditory nerve. CLARION is indicated for use in postlinguistically deafened adults, 18 years of age or older, with profound, bilateral sensorineural deafness (greater than or equal to 90 dB), who are unable to benefit from appropriately fitted hearing aids. Lack of aided benefit from a hearing aid is defined as scoring 20% or less on tests of open-set sentence recognition (i.e., CID Sentences). Additionally, there should be no radiographic contraindications to receiver placement or electrode insertion.

III. DEVICE DESCRIPTION

CLARION converts sounds in the environment into electrical code and transmits this code to auditory nerves in the cochlea. Acoustic sound waves enter the system through the microphone located in the headpiece and are transformed into an electrical signal. This signal is sent to the speech processor via cable. The speech processor converts the electrical signal into a code that has been determined, through the device fitting process selecting among the choices offered by the Clarion, the one most useful for a given patient in achieving sound. Once processed, the code is returned to the headpiece via cable and transmitted across the skin via electromagnetic induction to the implanted device. The implanted device decodes

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the signal and delivers it to the array of electrodes positioned within the cochlea. The electrodes stimulate the auditory nerve fibers within the cochlea. Each electrode is programmed to receive the processed signals and is adjusted to deliver the electrical stimulation at levels appropriate for the individual. Depending on the particular signal being transmitted, specific electrodes are stimulated.

The CLARION System consists of both patient and clinician components.

Patient Components: Patient components include both internal and external parts: an implanted electronic device, which is surgically placed under the skin behind the ear; an external speech processor, usually carried on a belt or in a pocket; and a headpiece. Additionally, there are accessory items, such as auxiliary microphones, telephone pick-up coils, cable clips and carrying cases.

The ***implanted device*** includes a magnet, an electronic receiver/stimulator and an electrode array. Together, the electronic receiver package and electrode array are referred to as the Implantable Cochlear Stimulator (ICS). The magnet and receiver are contained in a hermetically sealed ceramic case, measuring 1.74 x 0.98 x 0.24 inches and weighing 0.43 ounces. The receiver accepts and decodes signals from the external components of the system and presents these signals to the electrode array in the cochlea.

The electrodes, composed of platinum-iridium (90:10) alloy, are housed in a silicone rubber carrier (electrode array) and extends from the ceramic case. The intracochlear electrodes are designed to be inserted approximately 25 mm into a normally patent cochlea. The electrode array is in a spiral configuration. The electrode array is molded in a tight spiral curve and is designed to lie near the medial wall of the scala tympani. The electrode array consists of 16 spherical contacts arranged in 8 near-radial bipolar pairs.

Stimulus output circuits are capacitively coupled. They have regulated output currents from 0.5 to 2500 μA in logarithmic steps. The eight independent channels operate simultaneously, and the receiver has a processing rate of incoming signals of 13,000 samples per second at a uniform amplitude resolution of plus or minus 3.5%. With sequential stimulation, biphasic pulses are delivered at a rate of 6,500 pulses per second.

The ***speech processor*** is a miniature computer that translates the incoming analog waveform into either analog or pulsatile electrical code (depending on the strategy that is chosen). The speech processor also houses patient adjustable controls, such as volume and sensitivity, and a switch for the patient to alternate between two speech coding strategies (if the patient wishes to do so). The speech processor measures 2.4 x 5.2 x 0.7 inches and is powered by a rechargeable battery pack. A fully charged battery provides an average of nine hours continuous use.

The clinician has the ability to program two different speech coding strategies into the

external speech processor. The patient has the capability to switch back and forth between the two strategies. The coding strategy that is chosen delivers either an analog or interleaved pulsatile stimulating waveform. Either waveform can be programmed to operate in a bipolar or monopolar stimulation mode. All of these aspects of the programming of the device are controlled by the external speech processor that provides power and data to the internal receiver.

The ***headpiece*** is held in place by a magnet that aligns itself with the magnet in the implanted device. It contains a microphone that picks up sounds from the environment and sends the sounds to the speech processor via a thin cable that connects the headpiece to the speech processor. In addition to the microphone in the headpiece, an auxiliary microphone is provided, so patients can select a microphone location according to their individual preference.

Clinician Components: Clinician components include 1) the Clinician's Programmer, a hardware/software system for conducting psychophysical measurements and configuring the patient's speech processor; 2) the Portable Cochlear Implant Tester, a hand-held electronic device for performing diagnostic tests on the implanted receiver and electrodes; and 3) the Surgeon's Kit containing a specialized electrode insertion tool to assist the surgeon in the insertion of CLARION's curved electrode array.

IV. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative treatments for profoundly deaf adults include conventional hearing aids, other cochlear implants (both those approved for commercial sale and those which are investigational), tactile devices, and the use of manual communication or other communication systems, such as cued speech. A tactile aid is an externally worn device that converts sound waves to mechanical vibrations or electrical stimuli. These vibrations or stimuli can be felt on the skin, providing an awareness of sound.

V. CONTRAINDICATIONS (FOR WARNINGS AND PRECAUTIONS, SEE ATTACHED LABELING)

Use of cochlear implants is contraindicated in patients in whom deafness is due to lesions of the acoustic nerve or central auditory pathway. It is contraindicated in patients who present with an active or chronic middle ear infection, and in patients whose preoperative radiographic evidence indicates cochlear ossification that would prevent electrode insertion. The device is further contraindicated in patients who have an absence of cochlear development, or who present with tympanic membrane perforation.

VI. POSSIBLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Insertion of the intracochlear electrode will destroy any prior residual auditory function in the implanted ear.

Implant patients will incur the normal risks of surgery and general anesthesia. The implantation of the ICS and electrode array involves major ear surgery which may result in infection, bleeding, numbness, inflammation or discomfort about the ear, dizziness (either transient or persistent), facial paralysis, disturbance of taste or balance, tinnitus or neck pain. If these conditions occur, they are usually temporary and subside within a few weeks of surgery. Rarely, cochlear implantation can result in injury to or stimulation of the facial nerve or in perilymph fluid leak. Inner ear fluid leak may result in meningitis.

Implantation of the internal device may cause infection that can usually be treated with conventional antibiotics, but in some instances removal of the device may be required. An implanted cochlear device results in a palpable lump behind the ear. Skin flaps covering the implanted receiver/stimulator portion of the device may be too thick, resulting in difficulty maintaining a good connection between the internal receiver and the external transmitter. The presence of a foreign body under the skin may result in irritation, inflammation, or breakdown of the skin in the area around the implanted device and may cause extrusion of the device. Such complications may require additional medical treatment, surgery, and/or removal of the device. Failure of the implanted device could require removal, replacement or a reduction of the number of electrodes in use.

The long-term effects of chronic electrical stimulation are unknown. Such effects may include new bone growth in the cochlea or deterioration of auditory nerve fibers. These effects may preclude replacement of the electrode array or lead to deterioration of the cochlear response.

VII. MARKETING HISTORY

Advanced Bionics Corporation was authorized to affix the CE mark (certificate of marketing approval throughout the European Union) to the CLARION system in December 1993. As of June 1, 1995, 18 patients have been implanted in Italy, 68 in Germany, 15 in England, 3 in Switzerland, 5 in France, 7 in Spain and 1 in Sweden. Advanced Bionics Corporation was issued a Notice of Compliance from the Medical Devices Bureau in Canada in October 1994. As of June 1, 1995, 5 Canadian patients have been implanted. Additionally, 3 patients have been implanted in Argentina. Overall, there is a total of 125 foreign implants. CLARION has not been withdrawn from any country for any reason related to the safety and effectiveness of the device.

VIII. SUMMARY OF STUDIES

A. Nonclinical Laboratory Studies

1. Microbiological

The following microbiological tests were performed:

a) Sterility Assurance: Ethylene oxide sterilization was performed on five ICS devices inoculated with $1.3x10^4$ organisms to verify sterilization efficacy. The units were sterilized with two hour gas exposure. Following cycle completion, which included seven days of incubation, the units were found to be sterile.

b) Ethylene Oxide Residual Analysis: Ethylene oxide (ETO), ethylene chlorhydrin (EC) and ethylene glycol (EG) were extracted by placing an ICS in purified water at room temperature for 24 hours. The residuals in the eluate were determined by gas chromatography. All residual values fell well below the allowable limit and met the required minimum for sterilant residuals.

c) Pyrogenicity: The extract from one ICS immersed in normal saline for one hour was injected into three rabbits. There were no signs of pyrogenicity.

2. Biocompatibility

The sponsor submitted adequate data from a series of in-vitro and in-vivo studies demonstrating the biocompatibility of the following tissue-contacting components of the device:

ICS - Receiver/Stimulator Portion

Alumina: The ICS utilizes a polycrystalline alumina ceramic receiver capsule to house the electronics of the device.

Titanium Nickel Alloy: The braze that joins the ICS ceramic receiver to the electrode is 70% titanium: 30% nickel alloy.

Niobium: The ICS's indifferent electrode is fabricated from 99.5% pure niobium metal.

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Epoxy: Epoxy is utilized to encapsulate the feed-through electrical components between the electrode array and receiver portions.

Silicone: The ICS is coated with silicone, with the exception of a portion of the niobium band.

ICS - Electrode Array Portion

Platinum-Iridium: The electrodes are comprised of 90% platinum and 10% iridium alloy.

Silicone: The electrodes are housed in a silicone rubber carrier that extends from the ICS receiver/stimulator. An additional silicone block is placed to add further protection for the electrode wires.

Silicone Sheating: A blanket of silicone mesh sheeting is glued to the ICS to overlay the electrode lead as it exits the ICS, serving as a protector.

Med-A: The silicone sheeting is glued to the ICS with a medical grade adhesive, Med-A.

External Headpiece Base

Cycolac: The headpiece is molded from a Cycolac T-1000F resin.

The following biocompatibility tests were conducted on the above mentioned components.

a) Cytotoxicity: A minimum essential medium (MEM) elution test evaluation of one ICS, one small and one large headpiece was conducted to evaluate each of these items under the MEM testing requirements. The extract from each item immersed in MEM culture media at 37°C for 24 hours was evaluated. Test extracts and negative and positive control cultureplates containing mouse fibroblast cells were incubated at approximately 37°C for 48 hours. The test articles did not produce evidence of cytotoxicity.

b) Genotoxicity: Normal saline extracts from a functional ICS, powered for 30 days, were prepared for use in the Salmonella Reverse Mutation Assay (Ames Test). The extract tested against five tester strains was found to be non-mutagenic.

c) Acute Systemic Toxicity: Saline, cottonseed oil, ethanol and

polyethylene glycol extracts from an ICS were injected into groups of mice (each group consisting of five mice). The mice were observed for 72 hours. There were no signs of toxicity.

d) Intracutaneous Toxicity: Saline, cottonseed oil, ethanol and polyethylene glycol extracts from an ICS were injected intracutaneously into four rabbits. The rabbits were observed for 72 hours. There were no signs of irritation in the test sites.

e) Muscle Implantation Test: Three ICS devices and three negative controls were implanted intramuscularly in three rabbits for 90 days. There were no adverse effects. The ICS devices did not produce significantly greater biological reactions than did the negative controls.

f) Hemolysis: Saline extracts from an ICS and small and large headpiece were shown to be non-hemolytic.

g) Sensitization: Saline and cottonseed oil extracts from an ICS and small and large headpiece were shown to be non-sensitizing (Magnusson & Klingman maximization method). Positive controls validated the test procedure.

h) Corrosion: A study utilizing a combination of six functional and four demonstration ICS devices was conducted. The ICS devices were soaked in saline at 37°C, while delivering an output stimulus to the functional ICS devices. The stimulation waveform produced the maximum allowed charge density for an electrode ($300\mu C/cm^2$/phase).

Analysis consisted of microscopic and scanning electron microscopy (SEM) examination, monitoring of electrode impedances, and analysis of the solution in which devices were soaked for the presence of Aluminum (Al), Nickel (Ni), Niobium (Nb), Platinum (Pt) and Titanium (Ti). No detectable amount of Pt, Al, Ni or Ti was observed in the test solutions at the completion of a three- and six-month test cycle. Trace amounts of Nb (indicating an average of <300 μg of Nb per device) were detected in these two sample sets. Light microscopy and SEM were used to evaluate the surface of the Nb indifferent electrode ring and the interface between the ring and the ceramic ICS enclosure. No evidence of corrosion was visible in these structures. The absence of soluble corrosion products from the device, together with the biological testing data, demonstrated biocompatibility.

The sponsor changed silicone suppliers (from Dow Corning to Nu-Sil) after

the above studies had been completed. Therefore, FDA requested that the sponsor conduct three further tests to demonstrate the equivalence of the chemical structure of the original silicone and the Nu-Sil product. These three tests were tests of cytotoxicity, irritation, and sensitization. There were no adverse reactions demonstrated from the replacement silicone. The results of these three tests, plus FDA's review of the Master File which describes the chemical attributes of the Nu-Sil product, leads FDA to conclude that the chemical structure of the Nu-Sil product is equivalent to the Dow Corning product for this use.

3. Electrode Insertion and Cochlear Histopathology

The design of the CLARION electrode array resulted from a series of chronic in-vitro and in-vivo implant studies. The opportunity to study the temporal bones or auditory central nervous system of deceased CLARION patients has not presented itself at the time of this writing.

Insertion studies in human cadaver temporal bones were conducted to evaluate the incidence of traumatic damage resulting from the surgical introduction of a spiral electrode array (Ref. 1,2). These studies evaluated both the possibility of insertion trauma and the reliability of electrode contact positioning. In these studies, the restricted surgical view and approach were maintained to reflect the actual insertion process. The studies were conducted with an intracochlear electrode array identical to the CLARION electrode array in that it was molded with a spiral shape reflecting the appropriate dimensions of the human scala tympani and incorporating a vertically oriented central rib to determine the structural characteristics of the molded insert. Microdissection of each temporal bone followed insertion of the electrode array. The trials found that surgical application of these spiral electrodes did not result in fracture of the osseous spiral lamina, tearing of the basilar membrane or observable damage to the spiral ligament. Electrode contacts varied in lateral position by an average of less than 100 microns.

4. Measurement of DC Levels

Direct current (DC) is potentially damaging to neural tissue. The CLARION ICS has been designed to block direct-current stimulation. The design utilizes ceramic capacitors that are placed in series with each of the 16 output leads.

The leakage characteristics of the series output capacitors are specified by the manufacturer to be less than 1 nA/V. For the worst-case situation within the Clarion strategies, where a compliance voltage of 7 V could be reached, this corresponds to a maximum of 7 nA of leakage current. This capacitor

specification is worst-case and typical leakages are less. A test was performed, using a picoammeter, to monitor the actual direct currents that occur. These currents were found to be less than 0.1 nA on all outputs. The measurement noise level for this test was approximately 0.05 nA.

5. Electromagnetic Susceptibility

a) Near-Field ICS Testing: An ICS was placed in an electric field between two 7-cm square copper plates separated by 5 cm. The field was swept through the frequency range of 2 to 500 MHZ at an electric field strength of 340 V/m. The ICS operated normally under these conditions.

An ICS was placed in a magnetic field produced by a single-turn loop. Within each of 6 frequency bands covering the frequency range of 2 to 560 MHZ, the field strength was increased until the ICS stopped working. With one exception, susceptibility levels varied from 1.3 to 10.3 A/m. In the band of 10.3 to 11.1 MHZ, the ICS failed at 0.03 A/m.

b) System Testing: A complete patient system, consisting of an ICS, Speech Processor, headpiece and cable, was tested to evaluate the effects of radiated electromagnetic fields. The ICS was immersed in saline to simulate body tissue characteristics with a monitoring system established using a fiberoptic line to exit the testing field. Testing was conducted from 10 kHz to 1 GHz at electric field strengths of 0.5 to 7.0 V/m in a shielded room. The system was required to exhibit no loss of telemetry during exposure and to function electrically at the completion of testing. The system passed the electromagnetic susceptibility test, including the range used in cellular phones (800-900 MHZ).

6. Environmental Stress and Wear

A battery of engineering tests was performed on a group of ICSs at the component, sub-assembly, device and system level. Each sample was tested before and after each test. At the completion of each test, the characteristics of each element were measured and found to be the same as pre-test output characteristics.

a) Life Test - Accelerated High Temperature: Eleven ICS chips (VLSI) and 20 ICS hybrid assemblies were subjected to over 1,000 hours of life testing at a temperature of 125°C. Units were

electronically tested at weekly intervals. At the completion of the test, all units were tested for electrical functionality. All units passed.

b) Helium Leak (Hermeticity): All ICS units were 100% tested at the time of manufacture for hermeticity (this practice continues as part of the applicant's Good Manufacturing Practices). Each unit was placed in a ceramic case assembly and welded in an atmosphere of an inert gas mixture that included helium. Prior to final sealing, each feed-through, feed-through/header assembly, ceramic case and case band assembly was checked individually for hermeticity (leak rate less than 1×10^{-9} cc-atm/sec of helium). Only units that passed the helium leak test proceeded to final production devices.

c) Electrostatic Discharge (ESD): Two speech processors (SPs), Clinician's Programmers (CPs) and Battery Chargers (BCs) were subjected to ESD testing at levels of 5, 10, 15, 20 and 25 kilovolt (kV) peaks. After each shock, devices were evaluated for both soft (loss of performance) and hard (component damage) failures. Devices were required to exhibit no soft failures up to 15kV and no hard failures up to 25kV. All units passed.

d) Temperature Shock/Cycling: Two ICSs, SPs, CPs and BCs were subjected to thermal shock/cycling for 10 cycles. One thermal cycle was comprised of placing the device in a preheated chamber for the designated minimum time and then immediately transferring the device into a chamber that had been pre-cooled for the minimum designated time, as shown in Table 1

Table 1

	Chamber 1	Chamber 2
ICS	125°C(+10°C/-2°C) 5 minutes	-55°C(+2°C/-10°C) 5 minutes
SP	65°C(+0°C/-5°C) 25 minutes	-40°C(+0°C/-5°C) 25 minutes
CP	60°C(+5°C/-0°C) 20 minutes	10°C(+0°C/-10°C) 20 minutes
BC	65°C(+0°C/-5°C) 15 minutes	-30°C(+0°C/-5°C) 15 minutes

At the completion of testing, the ICS (receiver/stimulator) was evaluated for hermeticity. All devices were visually inspected and tested for electrical functionality. All devices passed.

e) Temperature Storage: Two of each device were subjected to high and low

temperatures, as shown in Table 2, for 96 hours at each temperature:

Table 2

	HIGH degree Centigrade	LOW degree Centigrade
ICS	+60°	-10
SP	+60°	-25°
CP	+45°	-9°
BC	+65°	-40°

At the completion of the test, the devices were electrically tested for functionality. All devices passed

f) Humidity Exposure: Two SPs, CPs, and BCs were subjected to 90% - 95% relative humidity at 40°C for 96 hours. Devices were evaluated at the completion of the testing for corrosion and electrical functionality. All devices passed.

g) Mechanical Vibration: Two ICSs, SPs, CPs, and BCs were subjected to sinusoidal vibration at a level of 10G's (2G's for the CPs) over a frequency sweep of 5Hz to 2000Hz to 5Hz on three axes. Devices were electronically tested for functionality at the completion of the testing. All devices passed.

h) Mechanical Drop: Two ICSs were dropped from 6-inch heights and two SPs, and BCs were dropped from 36-inch heights onto linoleum covered concrete. At the completion of testing, devices were visually inspected for damage and tested for electrical functionality. All devices passed.

I) Mechanical Shock Testing: Two ICSs were subjected to mechanical shock testing using a shock level of 100G's (±25G's), half-sine pulse, with a pulse duration of 5 ms (±2 ms). One shock was applied in each X, Y, and Z axis with complete electrical testing after each shock. After testing was completed, the hermetic seal was evaluated and physical integrity was examined under 30X magnification. No physical anomalies were identified, hermeticity was maintained and electrical performance was verified.

Two SPs and BCs were subjected to shock testing using a shock level of 185G's, half-sine pulse, with a pulse duration of 0.5 ms to 1.0 ms. One shock was applied in each of six mutually perpendicular axes. At the completion of testing, devices were visually inspected and tested for electrical functionality. All units passed.

j) Shipping Damage: One ICS, SP, CP and BC were packaged for standard shipment and subjected to the NTSA Project 1A Test Program. Upon

completion of the testing and inspection of the packaging, devices were tested for total functionality and visually inspected for damage. All devices, with the exception of the CP, were fully functional at the completion of the test. The CP exhibited a stuck micro-switch actuator arm. The CP was modified slightly to allow more freedom of movement of the micro-switch actuator arm. Subsequently, in over 25 actual shipments of CPs in the United States and Europe, this failure mode has not reoccurred.

k) Shelf Life: A long-term evaluation was conducted on two ICSs over the two years and eight months since their date of manufacture. Original electrical testing included a voltage level test and a standard electrical functionality test. No appreciable changes in performance occurred in the two devices since the date of manufacture.

l) Electrode Array: Four electrode arrays were subjected to the following testing:

Handling/Pull: Six drops of the ICS in six different positions while inserted in an electrode insertion tool (i.e. the ICS was dropped with the fantail portion pointing downwards, with the back portion pointing downwards, with the underside facing downwards, with the frontside facing downwards, and then with each of the two side edges pointing downwards).

Electrode Twist: Fifty cycles of twisting the electrode array two full turns in each direction.

Electrode Flex: Fifty cycles of flexing the spiral end of the array over the fantail portion.

Mechanical Performance: Ten cycles of insertion and re-insertion of the electrode array into the electrode insertion tube.

Fantail Flex: Five cycles of fully flexing the fantail portion of the electrode array back and forth over a 0.160 inch radius tool.

All electrodes passed the electrical testing at the completion of the tests. Visual examination revealed no areas of damage to the electrode array.

m) Electrode Array with Protector: Five electrode arrays with electrode protectors were subjected to the following testing:

Fantail Flex: Five cycles of fully flexing the fantail portion of the

electrode array back and forth over a 0.160 inch radius tool.

Handling/Pull: Six drops of the ICS in six different positions while the electrode array was inserted in the electrode insertion tool (same positions as described, above).

All electrodes passed the electrical testing at the completion of the tests and visual examination revealed no areas of damage to the electrode array.

7. Failure Modes and Effects Analysis

The predicted reliability of the ICS, SP and headpiece assembly was assessed utilizing failure modes and effects analysis (FMEA). Analyses did not reveal the presence of a failure that could lead to a life-threatening or hazardous situation.

ICSs have been implanted for a period in excess of four (4) years. From March 1991 through June 1, 1995, 273 devices have been implanted worldwide. During this period, there have been two electronic device failures (0.7% of the total number of devices implanted).

B. Clinical Investigations

1. Patient Inclusion and Exclusion Criteria

Subjects selected for the study included adults, 18 years of age or older, who demonstrated postlinguistic onset of bilateral profound sensorineural deafness ($\geq$90 dB) and who had never previously used a cochlear implant. The subjects demonstrated little to no benefit from conventional hearing aids. "Little benefit" from hearing aids was defined as a 10% or less score on a open-set word recognition test and a 20% or less score on a test of open-set sentence recognition in the best-aided preoperative test condition.

Exclusionary criteria included the following: acquired prelingual or congenital onset of deafness; medical or general health conditions that present risks to surgery; evidence of acute or chronic external or middle ear pathology; radiographic evidence of complete bilateral cochlear non-patency or anatomic deformity that would prevent electrode insertion or receiver placement; a period of less than six months elapse time since the onset of deafness; and inappropriate patient expectations regarding the potential benefits of the device.

2. Study Population

The study population utilized in the development of efficacy outcome data (see "Clinical Study Results") is based on the results reported in the PMA Clinical Update Amendment (dated January 20, 1995). The study population represents 68 patients who completed their six month audiological testing as of October 25, 1994. All patients for whom clinical outcomes are described have satisfied the protocol inclusion and exclusion criteria.

As of October 25, 1994, implantations occurred in 115 patients, 51 males and 64 females. According to medical charts, audiological records and self-reported histories, most patients experienced the onset of hearing loss in both the implanted ear and non-implanted ear in young adulthood. The mean age at onset of deafness in the implant ear was 42 years, with a range from 6 to 75 years of age. The mean duration of deafness was nine years, with a range of 0.5 to 42 years. The mean age at time of implant was 51 years, with a range of 19 to 80 years. No patients were able to achieve meaningful levels of sound-only speech recognition with hearing aids prior to implantation.

Of the 115 patients implanted as of October 25, 1994, 82 patients completed the three month and 68 patients completed the six month audiological evaluation. The mean duration of stimulation was 14.3 months, with a range of 0.6 to 40.4 months.

All patients implanted worldwide as of June 1, 1995 (148 U.S., 125 Foreign), have been considered in the analyses of device safety. The analyses of device effectiveness, however, considered study subjects who completed their six month audiological evaluations as of October 25, 1994 (e.g. the 68 patients noted above).

3. Investigators and Number of Investigational Subjects

As of October 25, 1994, 115 patients were implanted at 17 investigational sites in the United States.

4. Statistical Analysis

Device effectiveness was measured using a within subject, repeated-measures design with the patient serving as his or her own control. A range of improvement in auditory communication skills was expected with use of the implant. A patient was considered to have improved his/her performance if his/her postoperative score exceeded the preoperative score by a predetermined "critical difference". Critical difference scores are defined as

the smallest amount of improvement in performance that can be detected with a statistical power of 0.90 when alpha = 0.05.

A variety of tests was selected to assess device effectiveness. After testing the significance of improvement for each subject on each test (i.e., the "critical difference" for that test had to be exceeded in order to be considered as a significant improvement), the results were pooled across subjects to obtain an overall estimate of the percentage of patients improving in each category of performance.

Preoperatively, for the purposes of evaluating benefit with conventional aids and documenting aided speech recognition ability, all patients were fit with conventional amplification and evaluated in the "best-aided condition." All patients were administered a series of speech perception tests. The same audiological tests were performed at regular intervals postoperatively to measure performance over time. Pre-implant scores served as a control condition for within subject evaluation of efficacy claims. All studies were completed according to the clinical study protocol.

Gender-related differences were not observed with regard to the safety of the device. The sponsor noted that the available U.S. statistics on hearing loss do not make distinctions between pre- and postlingual deafness or the prevalence of deafness according to gender, race or ethnicity. Therefore, the sponsor was unable to comment on whether the ratio of men versus women in the CLARION study (there were 51 males and 64 females) reflects the distribution of profound sensorineural deafness for gender, ethnic group, or other population characteristics.

5. Evaluation Measures

Efficacy results have been divided into three categories: primary objectives, secondary objectives, and self-assessment of overall communicative ability. Primary objectives are represented by tests of speech recognition. Speech recognition was assessed with lipreading, without lipreading and over the telephone. The ability to understand speech in the auditory only condition (speech recognition without lipreading) represents the ultimate goal of cochlear implantation. This ability provides patients with the maximum opportunity to participate in the hearing world.

Secondary objectives include those functions that require less auditory discrimination ability and are represented by tests of awareness of speech and sounds, and tests of recognition of familiar sounds and warning signals.

Primary measures provided the basis for generating the efficacy outcomes that are reported in this summary and in the device labeling as "Clinical Study Results." Supporting measures offered additional evidence in support of the treatment effects but were not utilized in the effectiveness outcome discussed in the labeling.

The following table (Table 3) presents the outcome measures utilized to assess patient performance. The measures used to substantiate the "Clinical Study Results," that appear in the labeling for this device, are in bold-face type and marked with a (●).

Primary Objectives	Primary Measure(s)	Supporting Measures
Speech Recognition with Lipreading	CUNY Sentences, Vision Only ●**CUNY Sentences, Sound + Vision** CUNY Sentences Enhancement	Speech Tracking, Vision Only Speech Tracking, Sound + Vision Speech Tracking Enhancement
Speech Recognition without Lipreading	●**MAC CID Sentences** ●**MAC Monosyllabic Words (NU-6)**	MAC Spondee Recognition CUNY Sentences, Sound Only Speech Tracking, Sound Only Live Voice Test Battery
Speech Recognition over the Telephone	●**Overlearned Sentences Without Topic** SPIN Sentences	Overlearned Sentences with Topic
Secondary Objectives		
Awareness of Speech and Sounds	●**Pure Tone Average Threshold** ●**Speech Detection Threshold**	Most Comfortable Loudness Levels Speech Reception Thresholds
Recognition of Familiar Sounds and Warning Signals	●**Warning Signals**	Familiar Sounds
Discrimination of Prosodic Features	MAC Question/Statement MAC Noise/Voice	MAC Spondee Same/Different MAC Noise/Voice
Discrimination of Segmental Features	MAC Initial Consonants MAC Vowels	MAC Final Consonants MAC Four Choice Spondees
Speech Discrimination over the Telephone	Numbers Test	Coded Speech
Self-Assessment		
Overall Communicative Ability	●**PIPSL Understanding Speech with Visual Cues** ●**PIPSL Understanding Speech with No Visual Cues** PIPSL Intensity	PIPSL Environmental Sounds PIPSL Response to Auditory Failure PIPSL Personal

6. Results of Testing

Statistical analyses were performed to determine the significance of each preoperative to postoperative comparison on each measure. Outcome measures are expressed as the number of patients, and the percentage of patients who are represented by that number, performing significantly above their pre-implant scores in the best aided condition or significantly above their scores with the implant "off".

The critical difference scores (the smallest amount of improvement in performance that can be detected with a statistical power of 0.90, when alpha = 0.05) were used in the analyses of each clinical test to establish the number and percentage of patients who exhibited significant improvements as a result of treatment with CLARION. The "Clinical Study Results" are based on the 68 patients who had completed six month audiological evaluations. The results are reported as the number and percentage of patients who improved in their postoperative performance as compared to their preoperative performance (i.e., they exceeded the critical difference score for that particular test in the postoperative condition). The results are also reported as the range of outcome scores for each primary test measure. They are reported as the number and the percentage of patients achieving scores from the low-, mid-, and high-range of outcomes.

Analyses of the data demonstrate that the greatest gains in patient performance occur between the initial fitting and the six month evaluation. Cohort analyses of the 46 patients who had completed their 12 month testing as of October 25, 1994, reveal that there is no statistically significant difference between scores at 6 and 12 months.

A description of each of the test materials is provided below. Following the description is the statement, which appears in italics, that FDA approves for the sponsor to use in labeling materials. These outcome statements reflect the actual scores obtained by patients in the clinical trial, and the number of patients who were administered the test item. Although 68 subjects received the 6 month post-operative audiological test battery, not all subjects were given all tests at both the preoperative and the postoperative visits. This discrepancy occurred because some subjects were part of an earlier protocol that did not require testing as extensive as that in the later, revised protocol. Only patients who received the test both preoperatively and postoperatively are reported in the clinical outcome scores listed, below.

a) **Awareness of Speech and Sounds**

The primary measures utilized to assess awareness of speech and sounds were soundfield pure tone average thresholds (PTA) and speech detection thresholds (SDT).

The PTA represents the average warble tone thresholds at 500, 1,000 and 2,000 Hz. The PTA serves as an index to determine whether sounds within a specified loudness range are detectable by patients. Moderate sounds occur at 70 dB SPL or less and represent comfortable listening levels.

SDTs are used to determine whether speech sounds within specified loudness ranges are detectable by patients. Moderate speech occurs at 75 dB SPL or less.

Sixty-eight subjects (100%) detected speech and sounds at comfortable listening levels. (68 subjects tested)

b) **Recognition of Familiar Sounds and Warning Signals**

A subset of eight warning signals from the MAC Familiar Sounds test was the primary measure for the recognition of environmental sounds. Sounds are presented in an open-set format at normal listening levels (63 to 68 dBSPL). Based on auditory input only, patients are asked to identify the sounds.

Fifteen subjects (28%) demonstrated improvement in the recognition of familiar warning signals compared to aided pre-implant performance. Preoperatively with hearing aids, 23 subjects (43%) identified half or more of familiar warning signals. Postoperatively with the implant, 47 subjects (89%) identified half or more of familiar warning signals. (53 subjects tested)

c) **Speech Recognition with Lipreading**

The primary measure of speech recognition with lipreading was CUNY Sentences. CUNY Sentences are presented in the vision-only and sound-plus-vision conditions via computer controlled laser disc. The difference in scores between these two conditions, referred to as enhancement, represents the treatment effect. Measurements document both the overall level of speech recognition with lipreading and the enhancement produced.

The CUNY consists of 48 sentence lists. Three lists are presented per test condition: sound-plus vision and vision-only. Each list includes 12 sentences which are comprised of 102 words for a total of 306 words per condition tested. All words accurately repeated verbatim are marked as correct for a total percent correct score.

Fifty-eight subjects (87%) improved their communication ability when the device was used in conjunction with lipreading compared to aided pre-implant performance. Fifty-six subjects (84%) achieved scores over 50% on sentences with lipreading. Forty-nine subjects (73%) achieved scores over 75% on sentences with lipreading. Thirty-four subjects (51%) achieved scores over 90% on sentences with lipreading. (67 subjects tested)

d) **Speech Recognition without Lipreading**

The primary measures were the MAC open-set tests of auditory only speech recognition, CID Sentences and Monosyllabic Words (NU-6). These measures are the tests most frequently utilized in the evaluation of cochlear implant patient performance.

CID Sentences combine two lists from the Central Institute of the Deaf (CID) Everyday Speech Sentences, for a total of 100 keywords. Patients are required to repeat the sentences and keywords are marked as correct for a percent score. The NU-6 measure consists of 50 words from the Northwestern University Auditory Test #6. Patients are required to repeat the word spoken for a percent correct score.

Fifty subjects (74%) demonstrated improvement in open-set sentence recognition without lipreading compared to aided pre-implant performance. Fifty-one subjects (75%) achieved scores over 20% on sentences without lipreading. Thirty-five subjects (51%) achieved scores over 80% on sentences without lipreading. Seventeen subjects (25%) achieved scores over 95% on sentences without lipreading. Seventeen subjects (25%) scored less than 20% on sentences without lipreading. (68 subjects tested)

Forty-seven subjects (69%) demonstrated improvement in open-set monosyllabic word recognition without lipreading compared to aided pre-implant performance. Thirty-four subjects (50%) achieved scores of 30% or greater on monosyllabic words without lipreading. Twenty-three subjects (34%) achieved scores over 45% on monosyllabic words without lipreading. Eighteen subjects (26%)

achieved scores of 50% or greater on monosyllabic words without lipreading. (68 subjects tested)

e) **Speech Recognition over the Telephone**

One primary measure of speech recognition over the telephone was Overlearned Sentences without Topic. Overlearned Sentences are taken from a series of lipreading exercises intended to represent everyday phrases. There are 10 sentences with a total of 50 keywords. The patient is required to repeat the sentence that the tester has spoken over the telephone. Each keyword correctly repeated is marked as correct, for a percent correct score.

Forty-three subjects (64%) demonstrated improvement in open-set sentence recognition over the telephone, compared to aided pre-implant performance. Thirty-six subjects (54%) achieved scores over 65% on sentences heard over the telephone. Twenty-seven subjects (40%) achieved scores over 80% on sentences heard over the telephone. Eighteen subjects (27%) achieved scores over 95% on sentences heard over the telephone. (67 subjects tested)

f) **Self-Assessment of Overall Communicative Ability**

The primary measures for self-assessment were taken from the Performance Inventory for Profound and Severe Loss (PIPSL): Understanding Speech with Visual Cues, Understanding Speech with No Visual Cues and Intensity. Patients rank their response according to a 7-point scale ranging from 0 for "never" to 6 for "always". The overall scores for each of the categories are expressed as a numerical score derived from the average of the ranked responses.

Fifty-one subjects (75%) self-assessed their ability to communicate without lipreading as improved compared to aided pre-implant performance. Fifty-eight subjects (85%) self-assessed their ability to communicate with lipreading as improved compared to aided pre-implant performance. (68 subjects tested)

C. Summary of Safety Data

The following is a discussion of the anticipated and unanticipated adverse events that occurred during the clinical study using the Clarion Multi-Strategy Cochlear Implant. A discussion of the potential adverse effects associated with major ear surgery and the implantation of a cochlear implant is presented in section VI.

Medical and audiological tests and observations were conducted to establish the safety of the CLARION cochlear implant. The testing protocol focused on areas of possible adverse effects, both anticipated and unanticipated. The safety data are based on a total of 273 patients who were implanted worldwide as of June 1, 1995 (148 U.S. patients and 125 international patients).

1. **Anticipated Adverse Events**

a) **Lack of Magnetic Adherence**

There has been one case of an inability to achieve magnetic adherence between the external headpiece and the implanted device. The implant surgeon determined that the skin/muscle flap over the implanted device was too thick. Under local anesthesia in an out-patient procedure, the surgeon re-opened the incision and thinned the temporalis muscle lying over the device. A Special Bulletin was sent to all CLARION implant surgeons on January 13, 1993. Since that time, there have been no instances of surgical revision due to flap thickness. The requirements for appropriate placement of the receiver are described in the Surgeon's Manual.

b) **Vertigo and Tinnitus**

Physicians reported pre- and postoperative vestibular symptoms derived from patient interviews. In addition, patients were asked to report vestibular symptoms via questionnaires beginning at the 3-month postoperative evaluation.

Physicians reported on ninety-eight U.S. patients who were questioned about the presence or absence of preoperative vestibular symptoms. Eighty-three of the 98 patients (84%) reported no vestibular symptoms preoperatively. Postoperatively, follow-up data is available for 10 subjects at the 24-month time period and for 48 subjects at the 12-month follow-up evaluation. The remaining patients have follow-up times of 6 months or less. The data indicates that 26 of the 83 subjects (31%) who reported no vestibular problems preoperatively reported vestibular symptoms at one or more postoperative visits.

Patients reported slightly higher postoperative incidence of dizziness compared to the physician reports. However, none of the cases of dizziness were judged by the physician to be severe enough to require medical intervention.

Tinnitus was assessed by asking the patients, prior to implantation, if any tinnitus was present in the ear to be implanted. At the time of each follow-up visit (3- month, 6-month, and 12-month and 24-month), the patient was asked to report the presence or absence of tinnitus with the implant turned on versus the implant turned off. Forty-six patients from the U.S. clinical trial completed this evaluation at the 12-month follow-up. Of these, 20 patients reported no change in the presence or absence of tinnitus from the presurgical condition to when the device is turned off or turned on. Fifteen patients reported experiencing tinnitus prior to surgery and no tinnitus following implantation, either with the device on or off. Seven patients noted tinnitus prior to surgery and also post-surgery with the device turned off. These 7 patients experienced suppression of the tinnitus with the device turned on. Four patients reported experiencing no tinnitus prior to surgery, but they are experiencing tinnitus post-surgery both with the implant turned on and turned off. Thus, the majority experienced no change in their preoperative tinnitus or experienced a suppression of tinnitus when the device was turned on. The four patients that experienced tinnitus as a result of the implant are 8% of the total of the 46 patients who filled out the 12-month tinnitus questionnaire.

c) **Loss of Residual Hearing**

As anticipated, due to the length of the electrode array, all patients who had residual hearing preoperatively in the implanted ear lost that residual hearing postoperatively.

d) **Facial Nerve Stimulation**

Five patients in the U.S. Study experienced facial nerve stimulation when there device was initially activated. These cases have been resolved by re-programming the device.

e) **Inflammation**

There was one case of inflammation that occurred in a patient who had a thin skin flap. The inflammation occurred on the ridge where the receiver/stimulator could be felt through the skin. This was resolved through use of a half-shape magnet instead of the full magnet which holds the external transmitter in place over the skin that covers the internal receiver/stimulator.

2. **Unanticipated Adverse Events**

As of June 1, 1995, eleven cases of unanticipated adverse device effects have occurred among the total CLARION worldwide population of 273 patients. All are considered "major" medical/surgical complications and can be grouped into two categories: 1) electrode displacement, and 2) implanted receiver migration or extrusion. The total incidence of "major" surgical complications is 4%.

a) **Electrode Displacement**

There have been two cases of partial electrode displacement and one case of full electrode displacement into the middle ear space. In two of these cases, the devices were explanted and replaced, although the original devices were fully functional upon explant. In the third case, the patient has four active channels and continues to use his device without adverse effect.

Two Special Bulletins were sent to all CLARION implant surgeons on May 5, 1993 and September 23, 1993, respectively. These bulletins described the surgical technique required to successfully insert the CLARION electrode array. Additionally, a video tape demonstrating the use of the electrode insertion tool and proper insertion techniques was prepared and sent as an accompaniment to the Special Bulletin of 23 September 1993. Since the second surgical bulletin and video were sent, there have been no instances of electrode array displacement. The technique to properly insert the CLARION electrode array is described in the Surgeon's Manual.

b) **Device Extrusion/Migration**

There have been eight cases of migration, exposure, or extrusion of the implanted electronics package. Three cases occurred at foreign centers and five cases occurred at U.S. investigational sites. In six of these cases a revision surgery was performed in order to re-seat and secure the device in place. In another case, the device was explanted and a new unit was reimplanted. In the last case, the receiver was exposed through the skin and revision surgery was performed. Approximately one month after this revision procedure, the skin eroded. The surgeon determined that healing was unlikely with the device in place and explanted the unit, clipping and leaving the electrode in the cochlea in order to maintain passage for future reimplantation. In all eight cases, the original implanted device was

fully functional at the time of surgical revision. In all but one case of receiver migration/exposure, the device had been placed in a periosteum pocket without additional measures to secure the unit. It was determined that the primary cause of these migrations was surgical technique.

On August 10, 1994, Special Bulletin #4 was distributed to all CLARION surgeons, advising that a recessed bed to seat the receiver was required and that, after placement in the bed, cross sutures should be applied over the device. The technique to properly fix the implanted unit to avoid extrusion or migration is described in the Surgeon's Manual.

3. **Device Failures and Replacements**

As of June 1, 1995, there have been two electronic device failures. Each of these failures occurred in patients implanted at international CLARION centers. In one case, the issue is confounded because the failure apparently occurred during the course of a revision surgery due to an ICS migration. The device, fully functioning prior to the revision surgery, may have been damaged during the surgical procedure. In both instances, the patients have been reimplanted.

There have been a total of five device replacements. In two instances, as noted above, failed devices were explanted and new devices were implanted. In another instance, a device was replaced during the course of a revision surgery due to an ICS migration. The explanted unit was fully functional. In two cases, devices were replaced due to electrode displacement into the middle ear. In both cases, the explanted units were thoroughly tested and found to be fully functional. The long-term morbidity, both biological and electromechanical, for CLARION is unknown.

4. **Performance Degradation Over Time**

Adverse effects on audiological performance which might be expected from chronic electrical stimulation were not observed in the investigation; i.e., there was no evidence of deterioration in performance with continued use of the implant up to 36 months. Data analysis demonstrated that audiological performance with the cochlear implant remained constant or improved.

Electrical dynamic range, a measure of the difference between the amount of current needed to produce the softest sound the patient can hear and the amount of current needed to produce the loudest sound the patient judges to

be comfortable, was analyzed on a sample of patients and showed no change over time. Electrical impedance changes were also evaluated for the electrodes in each patient. No significant changes were recorded.

5. **Bone Growth**

Bone growth in cochlear implant patients may be caused by electrical stimulation and/or surgical trauma. An indication of bone growth would be a degradation in audiological performance with time, presumably a rise in hearing threshold or in the electrical impedances of the electrodes. As stated above, audiological performance with the implant remained constant or improved over the 36 months of the clinical study. No changes were noted in electrode impedance measurements.

IX. CONCLUSIONS DRAWN FROM THE STUDIES

The nonclinical and clinical data provide reasonable assurance that the CLARION Multistrategy Cochlear Implant System is safe and effective for its intended use, as stated in the approved labeling. See Attachment B.

X. PANEL RECOMMENDATIONS

On July 21, 1995 the Ear, Nose and Throat Devices Advisory Panel met to discuss PMA P940022. The Panel recommended that the application be found "Approvable With Conditions." These conditions included some changes to the labeling for the device and the addition of a postmarket study to monitor the ongoing safety and effectiveness of the device. This postmarket study was recommended because, although no change in electrical impedance or audiological performance was noted for the duration of the clinical trial, the CLARION cochlear implant does use a higher stimulation rate and has a higher total charge than the currently legally marketed cochlear implant. Therefore, the panel recommended that all patients in the clinical trial be followed for five years post-implantation to ensure that no future changes in performance occur.

Further, the panel recommended that the Clarion Multi-Strategy Cochlear Implant be approved for marketing for use in adult patients who obtain up to 20% open-set speech recognition on tests of sentence recognition (CID Sentences) in the preoperative "best-aided" condition. Although 25 patients had preoperative scores of up to 20% in the "best-aided" condition, it was difficult to determine the exact number of patients who actually demonstrated close to a 20% preoperative score in the ear that was implanted (most patients were tested preoperatively with their hearing aids either binaurally or with the aid worn in the better hearing ear, which was not the ear that was eventually implanted).

The critical difference score that was required to be achieved by a patient in the postoperative test condition before a score could be considered an improvement over the preoperative test condition for the CID Sentence test was determined by the sponsor to be 22%. Therefore, no patient was counted as having demonstrated postoperative improvement with the Clarion device unless they improved at least 22% over their preimplant score. Because of this, the sponsor maintained that there was no statistically significant difference between patients who scored 0% on the CID Sentence test and those who scored up to 20% (the inclusion criteria for use of the Clarion device requested by the sponsor) on this sentence test, either preoperatively or postoperatively.

The panel agreed with the sponsor that patients who score up to 20% on the preoperative "best aided" CID Sentence test, regardless of whether or not the "best-aided " score came from the ear to be implanted, the non-implanted ear, or binaurally, should be considered as no different from a patient who scores 0% on the preoperative measure, and should be considered as a candidate for use of the device.

However, to reflect the 25% of patients in this clinical trial who did not achieve at least a 20% postoperative score on the CID Sentence test, the panel also recommended that physicians, clinicians, and patients be informed of the low-end of performance by including this information in the "Results of the Clinical Study" section of all device labeling as well as in the Warning Section of the device package insert.

The panel also discussed whether or not to require surgeons and audiologists to be trained in the use of the Clarion device prior to implanting and programming the device. The final recommendation was to require training.

The panel gave this recommendation, following review of the surgical bulletin and video on the implantation procedure. The panel's recommendation took into account the uniqueness of the electrode insertion device and their understanding of the surgical difficulties in implanting and fitting the Clarion device.

XI. CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH) DECISION

CDRH concurred with the Panel's recommendation that the PMA be approved once the labeling changes had been satisfied and a postmarket study had been designed to monitor the ongoing safety and effectiveness of the device. FDA has concluded that with the final amendment submitted to the Agency on February 14, 1996 the requested labeling changes had been satisfied and a protocol for a well-designed postmarket study had been submitted.

A. Labeling: Patient Selection Criteria

FDA agreed with the panel that it was reasonable to accept the applicant's position that there was no statistical difference between a 0% score and a 20% score on the CID Sentence test and therefore, the inclusion criteria should include patients who obtain up to a 20% preoperative score on tape-recorded measures of sentence recognition (CID Sentences) in the preoperative "best-aided" test condition. However, FDA further determined that the applicant will report to FDA, as part of the postmarket study, the outcome measures of any newly implanted patients who have up to a 20% preoperative aided CID Sentence test score in the ear that was implanted. These subjects will be recruited from the investigative sites which participated in the clinical trial. The recruitment will last for three years from the date of the PMA application approval and each patient will be followed for one year postimplantation.

B. Postmarket Study

A representative sample of patients from the clinical trial will be followed for a period of five years from the date of implantation. In addition, FDA requested that the sponsor report and follow new patients who fall into the following categories: patients who are programmed in the Continuous Interleaved Strategy using bipolar stimulation; patients who are programmed in the Compressed Analog Strategy (either bipolar or monopolar); and patients whose Most Comfortable Levels of stimulation are greater than 1 mA. These new patients will be recruited for a period of three years from the date of the PMA application approval (from the investigative sites that participated in the clinical trial) and be monitored for a minimum of one year.

C. Training for Surgeons and Audiologists

Advanced Bionics has stated in the PMA Package Insert material that they "strongly recommend" that surgeons attend a training course. The PMA indicates that the Surgeon's Manual and the video describing the surgical procedure are provided to all physicians prior to the surgery. Advanced Bionics further states that the Package Insert, in its entirety, is included in the User Handbook, the Portable Cochlear Implant Tester Manual, the Surgeon's Manual and in the Audiologist's Manual.

The FDA understands that ENT surgeons are well educated in the anatomy of the ear and in surgical procedures involving care of the facial nerve and the facial recess approach to the round window. In addition, many residency training programs are part of cochlear implant teams and teach the physicians the proper implantation technique. The FDA believes that adequate steps

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have been taken by Advanced Bionics towards making the implant surgeon fully aware of his or her responsibility to be educated in the technique required to implant the Clarion Multistrategy Cochlear Implant. Therefore, FDA did not agree with the ENT Devices panel recommendation that training be required. The labeling will read that training is "strongly recommended."

The FDA is aware that Advanced Bionics will conduct training courses for physicians who wish to avail themselves of the opportunity. Training will also be offered to audiologists who wish to learn the programming of the device.

XII. APPROVAL SPECIFICATIONS

Directions for Use: See the labeling (Attachment 1)

Hazards to Health from Use of Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling (Attachment 1)

Postapproval Requirements and Restrictions: See approval order (Attachment 2)

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PACKAGE INSERT
CLARION™ MULTI-STRATEGY™ COCHLEAR IMPLANT SYSTEM

INDICATIONS: The CLARION™ Multi-Strategy™ Cochlear Implant, hereinafter referred to as CLARION, is intended to restore a level of auditory sensation to individuals with profound sensorineural deafness via electrical stimulation of the auditory nerve. CLARION is indicated for use in postlingually deafened adults, 18 years of age or older, with profound, bilateral sensorineural deafness (≥90 dB), who are unable to benefit from appropriately fitted hearing aids. Lack of aided benefit from a hearing aid is defined as scoring 20% or less on tests of open-set sentence recognition (CID Sentences). Additionally, there should be no radiographic contraindications to receiver placement or electrode insertion.

CONTRAINDICATIONS: Deafness due to lesions of the acoustic nerve or central auditory pathway; Active external or middle ear infections; Cochlear ossification that prevents electrode insertion; Absence of cochlear development: Tympanic membrane perforation.

ADVERSE EVENTS: Safety data are based on a total of 273 patients who were implanted during the clinical study (148 U.S. patients and 125 international patients) of CLARION. Not all subjects were evaluated for all effects. For example, 46 U.S. patients participated in a 12-month postoperative questionnaire and 98 U.S. patients were evaluated for symptoms of dizziness. The following adverse events occurred during the clinical study of CLARION:

- For all patients, implantation of the cochlear implant resulted in a palpable lump behind the ear.
- For all patients, insertion of the intracochlear electrode array resulted in the loss of residual hearing in the ear that was implanted.
- Five patients experienced device migration, one patient experienced device extrusion, and two patients experienced device exposure. These problems were due to improper surgical placement of the implant.
- Three patients experienced electrode displacement (one case of full displacement and two cases of partial displacement) due to improper use of the electrode insertion tool.
- Four patients experienced facial nerve stimulation. All cases of facial nerve stimulation were resolved through reprogramming of the device.
- Two patients experienced electronic device failures and required surgery to replace the device.
- Ninety-eight patients were evaluated for preoperative and postoperative vestibular symptoms. Follow-up time varied from six to 24 months. Of the 83 patients who reported no preoperative vestibular symptoms, 26 patients reported mild, fluctuating dizziness postoperatively. None of the cases of postoperative dizziness required medical intervention.
- Forty-six patients participated in filling out a tinnitus questionnaire at the 12 month postoperative follow-up. Four patients who reported experiencing no tinnitus prior to surgery reported tinnitus with the implant turned both on and off. Twenty-two patients who reported experiencing tinnitus prior to surgery reported no tinnitus postoperatively with the implant turned on.

- One patient experienced an inability to achieve magnetic adherence between the headpiece and the implant which was resolved by a surgical thinning of the flap over the implant.

- One patient experienced skin irritation over the implant.

POSSIBLE ADVERSE EVENTS: Although there were no reports during the clinical study of the following adverse events, these additional events are known to be possible adverse events associated with cochlear implants.

- Implant patients will incur the normal risks of surgery and general anesthesia.

- Major ear surgery may result in numbness, swelling or discomfort about the ear, disturbance of taste or balance, or neck pain. If these occur, they are usually temporary and subside within a few weeks of surgery.

- Rarely, cochlear implantation may cause a leak of the inner ear fluid which may result in meningitis.

- Implantation of the internal device may cause infection that can usually be treated with conventional antibiotics, but in some instances may require removal of the device.

WARNINGS:

- **Electrosurgical instruments** must not be used within the vicinity of a cochlear implant and/or its electrode system. Electrosurgical instruments are capable of producing radio frequency voltages of such magnitude that a direct coupling can effectively exist between the cautery tip and an electrode array. Induced currents could cause damage to the cochlear tissues or permanent damage to the implant.

- **Diathermy** must never be applied over the receiver/stimulator or electrode lead of the cochlear implant. High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant

- **Electroconvulsive therapy** must never be used on a cochlear implant patient. Electroconvulsive therapy may cause tissue damage to the cochlea or permanent damage to the implant.

- **Ionizing Radiation Therapy** cannot be used directly over the cochlear implant as it may damage the device.

- Exposure of the cochlear implant to a **Magnetic Resonance Imaging (MRI)** device may cause deleterious effects to the implant and to the patient. Individuals with a CLARION cochlear implant cannot undergo an MRI procedure or be in the same room with an MRI system, regardless of whether the system is in operation or not. The inability to undergo an MRI procedure prevents access to an important diagnostic modality.

  The effects of **cobalt treatment and linear acceleration** techniques on the implant are unknown.

- **Insertion of an intracochlear electrode** will result in the loss of any residual hearing in the implanted ear.

- The long term effects of **chronic electrical stimulation** are unknown. Such effects may include new bone growth in the cochlea or deterioration of the auditory nerves. These effects may preclude replacement of the electrode array or lead to deterioration of the cochlear response.

- **Electrode displacement** can occur if the electrode is not inserted properly. Surgeons should be proficient in the use of the electrode insertion tool.

- **Extrusion or migration of the implant** can occur if the device is not properly recessed into the mastoid bone. Surgeons should be skilled in the recommended surgical technique to implant CLARION.

- **Extreme direct pressure** on the implanted device, up, down, left or right may cause the implant to move and possibly dislodge the electrode array. The implanted device is surgically placed on the mastoid bone and is capable of withstanding the effects of running, exercise and normal activity. A direct hit by a hard object or sharp blow to the implant may damage the device. It is recommended that individuals participating in any type of contact sports wear a helmet or protective headgear. The surgeon or audiologist should be called if is suspected that the device has been damaged.

PRECAUTIONS:

- Static electricity has the potential of damaging the electrical components of a cochlear implant system. Care should be taken to avoid situations in which static electricity is commonly created, such as when pulling on and off clothes or walking across a wool rug. If static electricity is present, patients should touch something conductive (e.g., a metal object) before their cochlear implant device contacts another person or object.

- Airport or security metal detectors may be activated by the cochlear implant system; thus, it is advised that patients carry their "Patient Emergency Identification" card with them at all times.

- Cochlear implants do not restore normal hearing and benefits vary from one individual to another. Benefits range from the recognition of speech and sounds at comfortable listening levels to speech understanding with and without lipreading and over the telephone. There appears to be little correlation between the degree of benefit obtained from an implant and the cause of deafness.

- There are no definitive tests which can be administered prior to implantation that estimate the degree of benefit an individual may receive. Not all patients will achieve at least 20% on tests of open-set sentence recognition without lipreading (i.e., CID Sentences) with the implant. (Refer to Clinical Study Results)

- Implant recipients should only use the speech processor that has been specifically programmed for them by their clinician. Use of a different speech processor may be ineffective in providing sound information and may cause physical discomfort from overstimulation.

CLINICAL CONSIDERATIONS: Optimized hearing aid fitting and evaluation procedures are critical to the selection of suitable cochlear implant candidates. In order to ensure selection of appropriate candidates, hearing health care professionals should utilize clinically-accepted state-of-the-art amplification, diagnostic instruments and hearing aid fitting procedures.

When a patient is determined to be eligible for CLARION, the ear for implantation is selected. The following hierarchy of considerations is recommended:

- **Cochlear patency and the scala tympani.** The ear with the least cochlear ossification and the most normal appearing scala tympani, according to radiographic evidence is given primary consideration and takes precedence over other factors.

- **Residual hearing.** The ear with the poorest functional hearing is selected for implantation.

- **Duration of hearing loss.** If one ear has sustained deafness for a longer period of time than the other ear, the ear with the most recent onset of deafness is selected.

- **Age of onset.** Ears which have experienced prelingual or congenital loss should not be implanted. The patient should have a history of auditory perception and speech and language development.

- **Patient preference.** If both ears are equivalent in all regards, the patient's preference should be the determining factor in selecting the ear for implantation.

CLINICAL STUDY RESULTS: Clinical results were achieved in a study of postlingually deafened (≥90 dB) adults who were consecutively implanted with CLARION. Results are reported for the number and proportion of patients demonstrating statistically significant improvement and achieving a particular level of performance. Improvement results are based on comparisons to pre-implant data in the best aided condition utilizing critical difference scores. Critical difference scores were calculated using standard error of measure and power curves derived from published reliability data for the test measures. The study subjects were tested in quiet at normal conversational levels (50 - 55 dB HL) at six months of device usage.

- Sixty-eight subjects (100%) detected speech and sounds at comfortable listening levels. (68 subjects tested)

- Fifteen subjects (28%) demonstrated improvement in the recognition of familiar warning signals compared to aided pre-implant performance. Preoperatively with hearing aids, 23 subjects (43%) identified half or more of familiar warning signals. Postoperatively with the implant, 47 subjects (89%) identified half or more of familiar warning signals. (53 subjects tested)

- Fifty-eight subjects (87%) improved their communication ability when the device was used in conjunction with lipreading compared to aided pre-implant performance. Fifty-six subjects (84%) achieved scores over 50% on sentences* with lipreading. Forty-nine subjects (73%) achieved scores over 75% on sentences* with lipreading. Thirty-four subjects (51%) achieved scores over 90% on sentences* with lipreading. (67 subjects tested)

  *CUNY Sentences, representing standard everyday speech, presented via laser disk and requiring exact repetition.

- Fifty subjects (74%) demonstrated improvement in open-set sentence recognition without lipreading compared to aided pre-implant performance. Fifty-one subjects (75%) achieved scores over 20% on sentences* without lipreading. Thirty-five subjects (51%) achieved scores over 80% on sentences* without lipreading. Seventeen subjects (25%) achieved scores over 95% on sentences* without lipreading. Seventeen subjects (25%) scored less than 20% on sentences* without lipreading. (68 subjects tested)

  *CID Sentences, representing standard everyday speech, presented via monitored audio tape recordings and requiring recognition of key words.

- Forty-seven subjects (69%) demonstrated improvement in open-set monosyllabic word recognition without lipreading compared to aided pre-implant performance. Thirty-four subjects (50%) achieved scores of 30% or greater on monosyllabic words* without lipreading. Twenty-three subjects (34%) achieved scores over 45% on monosyllabic words* without lipreading. Eighteen subjects (26%) achieved scores of 50% or greater on monosyllabic words* without lipreading. (68 subjects tested)

  *NU-6 Words, representing single syllable words, presented via monitored audio tape recordings and requiring exact repetition.

- Forty-three subjects (64%) demonstrated improvement in open-set sentence recognition, over the telephone compared to aided pre-implant performance. Thirty-six subjects (54%) achieved scores over 65% on sentences* heard over the telephone. Twenty-seven subjects (40%) achieved scores over 80% on sentences* heard over the telephone. Eighteen subjects (27%) achieved scores over 95% on sentences* heard over the telephone. (67 subjects tested)

  *Overlearned Sentences, representing previously unknown, familiar phrases, presented over the telephone and requiring recognition of key words.

- Fifty-one subjects (75%) self-assessed their ability to communicate without lipreading as improved compared to aided pre-implant performance. Fifty-eight subjects (85%) self-assessed their ability to communicate with lipreading as improved compared to aided pre-implant performance. (68 subjects tested)

STORAGE: CLARION should be stored at temperatures in the range of 0° to 50° Centigrade (32° to 122° Fahrenheit).

HANDLING: Severe impact could damage the storage pack and rupture the sterile packaging. An impact with a force in excess of 85 pounds could fracture the ceramic case. Therefore, it is good practice to handle the package with the care appropriate to any implantable medical device.

SHELF LIFE: A "Use Before" date is located on the device packaging. This date is two years from the date of sterilization. The cochlear implant itself is not subject to aging.

STERILIZATION: CLARION is supplied in ethylene oxide sterile packaging with indicators of sterilization. Sterile packs should be carefully inspected to confirm that they have not been ruptured. Sterility cannot be guaranteed if the sterile package is damaged or opened.

INFORMATION FOR USE AND RECOMMENDED TRAINING: A Surgeon's Manual and a video describing the surgical procedure and insertion of the electrode are provided to all physicians prior to implantation. Physicians should be well versed in mastoid surgery and the facial recess approach to the round window. Physicians should be trained in the implantation procedure for the CLARION cochlear implant. Advanced Bionics conducts periodic training courses and strongly recommends that surgeons attend a training course. It is also strongly recommended that surgeons work with an audiology professional who has been fully trained on the proper fitting and adjustment of the CLARION cochlear implant.

An Audiologist's Manual is provided. Audiologists should be trained in the fitting of the CLARION cochlear implant. Advanced Bionics conducts periodic training courses for audiologists and strongly recommends that audiologists attend a training course. Additionally, there is a manual which describes the operation and use of the Portable Cochlear Implant Tester.

A pamphlet entitled "An Introduction to Cochlear Implants for Adults" is available to individuals inquiring about a cochlear implant. This pamphlet is designed to assist in answering basic questions that a prospective patient may have and to serve as a tool for professionals in patient screening.

Two manuals entitled "Patient Information Guide for Adults" and "CLARION User Handbook" are provided to the audiologist and should be given to all prospective candidates and CLARION recipients. The "User Handbook" describes how to use the external components of the CLARION system. The "Patient Information Guide" provides detailed information about CLARION, indications for use, benefits, risks, and what is involved in patient selection, surgical and out-patient procedures.

CAUTION: Federal law restricts this device to sale, distribution and use by or on the order of a physician.

For more information contact:
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Sylmar, CA 91342 U.S.A.
(818) 362-7588

CLARION™ Multi-Strategy™ Cochlear Implant System

Introduction to Cochlear Implants for Adults

CAUTION: Federal law restricts this device to sale, distribution, and use by or on the order of a physician.

Authorized to affix the CE mark in 1993.

CE

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This pamphlet is written for individuals who want general information about cochlear implants. It is designed to answer many of the most frequently asked questions and includes an overview of what a cochlear implant is, how cochlear implants work, who may benefit and what may be expected from evaluation through implantation. In particular, the CLARION™ Multi-Strategy™ Cochlear Implant System is described.

For more detailed information about the CLARION, indications for use, the surgical procedure, the rehabilitation process, benefits, risks, and possible adverse events, please refer to the *CLARION Patient Information Guide for Adults* and the *CLARION Package Insert*.

INTRODUCTION TO COCHLEAR IMPLANTS

A cochlear implant is an electronic device designed to provide useful hearing and improved communication ability to individuals who are profoundly hearing impaired and who derive limited benefit from hearing aids. Hearing aids make sounds louder and deliver the amplified sounds to the ear. However, for individuals with a profound hearing loss, even the most powerful hearing aids may not help in achieving speech recognition. Cochlear implants bypass the damaged parts of the ear and send electrical 'sound' signals directly to the hearing nerve.

Cochlear implant technology was first researched and developed in the 1960s and 1970s. Since that time, cochlear implant systems have continued to improve from the first single-channel systems to the more recent multichannel devices. Today, advances in computer hardware and software and sound processing technology have produced implant systems that provide better sound than ever before.

CLARION represents a new generation in cochlear implant technology. CLARION incorporates advanced computer technology, electronic circuitry and sound processing. This technology may provide CLARION users with improved and superior sound compared to earlier generation cochlear implant devices.

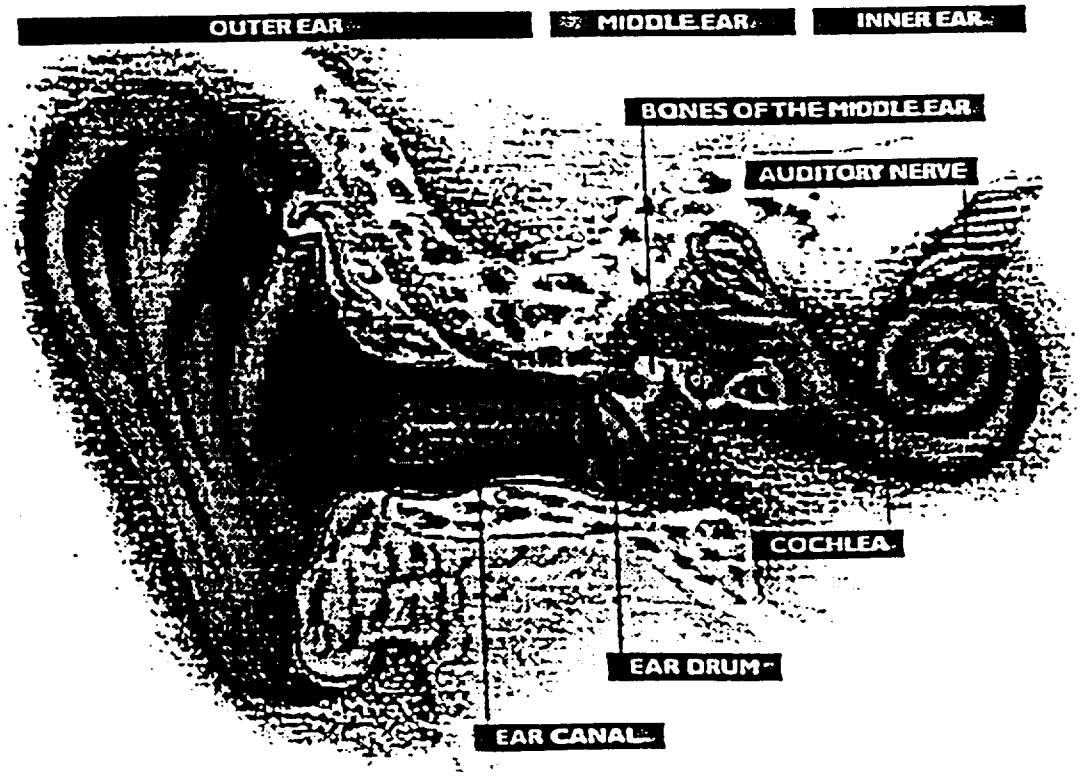
HOW WE HEAR

To understand how a cochlear implant works, it is helpful to have a basic understanding of how the ear normally functions to process sound.

Your ear is a remarkable mechanism which consists of three parts:

Outer ear:	the visible outer portion of the ear and ear canal
Middle ear:	the eardrum and three tiny bones
Inner ear:	the fluid-filled, snail-shaped cochlea which contains thousands of tiny hair cells

For you to hear, sound must pass through all three parts of the ear. The outer ear collects the sound and directs it through the ear canal to the eardrum in the middle ear. The sound waves strike the eardrum and cause it to vibrate. This vibration creates a chain reaction in the three tiny bones of the middle ear. Motion of these bones generates movement of the fluid contained in the snail-shaped cochlea. As the fluid begins to move, tiny hair cells lining the cochlea move back and forth to generate an electrical current. This electrical current stimulates the hearing (auditory) nerve which carries the signal to the brain where it is interpreted as sound.



THE HEARING IMPAIRED EAR

In many individuals with a profound hearing loss, the hair cells may be damaged or diminished. In these cases, there is no mechanism to initiate electrical impulses to the hearing nerve. Without these electrical impulses, the hearing nerve cannot carry messages to the brain. If there are not enough hair cells, even the loudest of sounds may not be heard. In many cases of mild to severe hearing loss in which some healthy hair cells exist, hearing aids may help. For individuals with a profound hearing loss who are unable to obtain benefit from conventional hearing aids, a cochlear implant may help.

COCHLEAR IMPLANTS ARE NOT HEARING AIDS

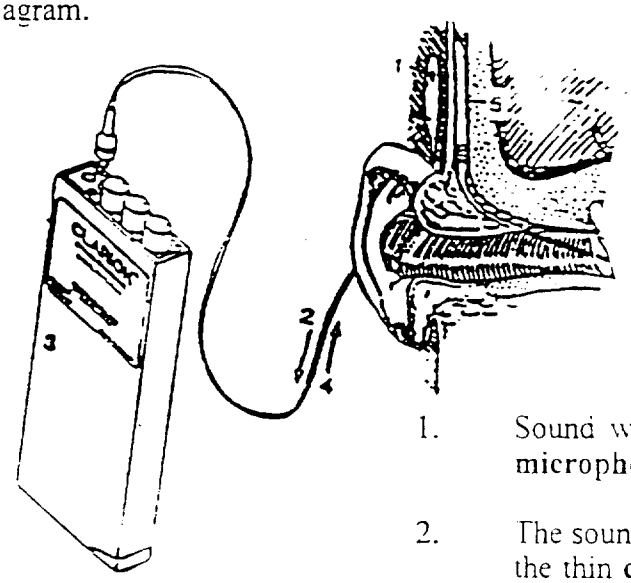
Hearing aids and other types of assistive listening devices make sounds louder and deliver these amplified sounds to the ear. Making sounds louder or increasing the level of amplification may not enable a profoundly deaf ear (in which the hair cells are damaged or diminished) to process sound. Cochlear implants bypass the damaged parts of the ear and stimulate the hearing nerves, allowing individuals who are profoundly hearing impaired to receive sound.

CLARION MULTI-STRATEGY COCHLEAR IMPLANT

CLARION is a new generation cochlear implant and incorporates some of the latest advances in electronic circuitry, computer technology and sound processing.

CLARION consists of both internal and external components. The internal parts include an implantable cochlear receiver/stimulator (ICS) which houses the electronics of the implant and 16 tiny wires bundled together, called the electrode array. The external parts include a battery powered speech processor, which is usually carried on a belt or in a pocket, and a headpiece, which is worn on the head just behind the ear.

CLARION converts speech and other sounds in the environment into electrical signals and sends these signals to the hearing nerve. Below is a step-by-step outline of how CLARION works to produce sound. Each numbered step corresponds to the number in the diagram.



1. Sound waves enter the system through the **microphone located in the headpiece.**

2. The sound is sent to the speech processor via the thin **cable** which connects the headpiece to the speech processor.

3. The **speech processor** converts the sound into a special signal. This conversion is accomplished through sophisticated software programs called speech processing strategies.

4. Once processed, the special signal is sent back up the same cable to the headpiece and transmitted across the skin via radio waves to the implanted device.

5. The **implanted device** receives the signal and delivers it to the array of electrodes positioned within the cochlea.

6. The **electrodes** stimulate the nerve endings within the cochlea causing electrical impulses to be delivered to the brain where they are interpreted as sound.

FEATURES OF CLARION

Choice of Speech Processing Strategies Today...

Speech processing is the method by which incoming sound is converted or 'processed' into a special electrical signal which is then interpreted by the brain. CLARION offers users a choice of two different speech processing strategies in the same speech processor. The user can choose the program that provides the best sound or switch between programs to maximize hearing. The programs in the speech processor can be modified as the needs of the individual change.

...and Tomorrow

Speech processing strategies are actually computer software programs. CLARION is designed to incorporate new software programs similar to the way software programs are added to a computer. There is no need for additional surgery or to replace expensive hardware with each new advance in speech processing technology. However, just as with computers, as cochlear implant technology continues to advance, it is possible that existing equipment would need to be replaced in order to take advantage of these changes.

Detailed Representation of Speech Sounds

CLARION processes and sends information to the inner ear at a high rate of speed, delivering a detailed representation of speech sounds. The CLARION speech processor contains a powerful microcomputer chip capable of transmitting up to 104,000 pieces of information per second.

Engineered for Safety

CLARION incorporates many features to maximize safety. CLARION allows testing of the implanted device during the surgical procedure and at any time after surgery. This feature assures the patient and physician that all components of the implant are functioning properly. The implant electronics include special components, called capacitive couplers, to prevent the leakage of direct current which could damage internal tissues. Additionally, both CLARION's internal electronics and the receiving coil are sealed within a single ceramic case to prevent breakage.

Engineered for Reliability

CLARION is manufactured by Advanced Bionics Corporation, a company dedicated to providing the highest quality products and services. Advanced Bionics is a spin-off from the second largest pacemaker manufacturer in the world.

FROM EVALUATION TO IMPLANT

Patient Selection Criteria: Your physician and the implant team can determine if CLARION is right for you. CLARION is designed for individuals with a profound, sensorineural hearing loss in both ears (90 decibels or greater). Normal speech and conversation usually occur at 50 to 60 decibels. The term sensorineural applies to individuals with "nerve deafness." Candidates are unable to understand speech through the use of hearing aids and have lost their hearing after some speech and language skills have been learned. In addition, candidates should be in good health and motivated to learn to hear again.

Evaluation: In order to determine if an individual is a candidate for CLARION, a complete hearing (audiological) evaluation is conducted by the implant center. This evaluation will assess the candidate's type of hearing impairment, level of hearing loss and performance with appropriately fitted hearing aids.

In addition to the hearing evaluation, the selection process includes other medical tests such as an ear examination and x-rays of the cochlea. Individuals are counselled with respect to the benefits and risks of a cochlear implant.

Surgery: Surgery is required to implant the internal components of the cochlear implant system. The surgery is performed under general anesthesia and typically takes between two and three hours. The procedure can be performed in either an inpatient or outpatient setting. Cochlear implant surgery carries similar risks to those associated with major ear surgery and general anesthesia. Your implant surgeon and audiologist will discuss with you all possible surgical risks.

Follow-Up: Typically, one to two days after surgery, patients return home for a period of four to six weeks to allow for complete healing around the surgical site. Most individuals return to normal activities within a week or two after surgery. After this healing period, patients return to the implant center to begin the process of "fitting" the external portion of the system. This procedure is usually performed by an audiologist who works as part of the implant team. The fitting process involves programming the device to meet each person's individual needs.

CLARION allows the audiologist the opportunity to program two speech processing strategies into one speech processor at the same time. Some individuals prefer one strategy, some prefer another, and others use more than one strategy depending on the listening environment. The audiologist will work with each individual to determine the most effective strategy or strategies.

During the first few months of cochlear implant use, minor speech processor adjustments are made. Thereafter, follow-up visits typically occur either on a six month or annual basis.

BENEFITS

Cochlear implants do not restore normal hearing and benefits vary from one individual to another. There are many factors which contribute to the degree of benefit obtained from a cochlear implant, such as how long a person has been deaf and the number of surviving hearing nerve fibers. A patient's motivation may also contribute to an implant's effectiveness. There appears to be little correlation between the degree of benefit obtained from an implant and the patient's cause of deafness. Unfortunately, there are no definitive tests that can be administered prior to implantation which estimate the degree of benefit an individual may receive.

The benefits of CLARION were demonstrated during a comprehensive clinical study of postlingually deafened adults (≥90 dB) who were implanted with CLARION at leading implant centers across the United States. Benefits included the following range of results:

- Recognition of speech and sounds at comfortable listening levels
- Improvement in speech understanding with lipreading
- Improvement in speech understanding and word recognition without lipreading
- Ability to use the telephone

RISKS

The risks of cochlear implant surgery are the same as those associated with any major ear surgery requiring general anesthesia. In addition, major ear surgery may result in numbness, irritation, swelling or discomfort about the ear. Dizziness, disturbance of taste or balance, ringing in the ears (tinnitus) or neck pain may also occur in some patients. If these occur, they are usually temporary and subside within a few weeks of surgery. In some cases, mild dizziness or balance problems may persist.

ADDITIONAL INFORMATION

The cochlear implant team is the best source of information about cochlear implants. Additionally, the CLARION *"Patient Information Guide for Adults"* and the *"Package Insert"* are available which include detailed information about indications for use, the results of the CLARION clinical study, the surgical procedure and surgical risks, the rehabilitation process, possible adverse events, warnings and precautions.

FREQUENTLY ASKED QUESTIONS

How long have cochlear implants been used?

Experimentation with electrical stimulation was first done by French researchers in the late 1950s. Since then, cochlear implants have been in development around the world.

Who developed and designed CLARION?

CLARION is the result of many years of extensive research and development and represents the cooperative efforts of the University of California, San Francisco, Research Triangle Institute, and the device manufacturer, Advanced Bionics Corporation.

How much does a cochlear implant cost and will insurance pay for it?

As with most medical prostheses, cochlear implants are expensive. Many insurance carriers provide full or partial coverage for cochlear implants and the associated costs. The amount of coverage depends on the specific insurance carrier. The implant center submits the proper documentation to the insurance carrier for approval. Additionally, reimbursement assistance is available for CLARION from the insurance reimbursement department at Advanced Bionics. The insurance department will work with the individual, the implant center and the insurance company to help potential implant users receive the maximum coverage available through their insurance carriers.

Are there any restrictions on physical activities?

The implanted device is capable of withstanding the effects of running, exercise and normal activity. However, precautions must be taken when participating in contact sports in order to avoid any blows to the head. Additionally, the external components of the system should be protected from moisture and breakage. The speech processor and headpiece must be removed before bathing or swimming or when participating in an activity where these components could get wet.

Is CLARION covered under warranty?

CLARION is designed to withstand the wear and tear of daily life. The implanted components are warranted for five years, while the speech processor has a three-year warranty. When the user first receives the system, spare batteries, cables and accessory equipment are provided. Over time, the batteries and cables may need to be replaced.

What is Advanced Bionics' commitment to the field of cochlear implants?

Advanced Bionics is a spin-off from the second largest heart pacemaker manufacturer in the world. Its experience in implantable prostheses and miniaturization demonstrates the Company's commitment to advanced technology. CLARION represents years of extensive research and development and the collaborative efforts of some of the world's leading research institutions in the field of cochlear implants. Ongoing research continues and Advanced Bionics is committed to maintaining its position at the forefront of new technology and development.

Advanced Bionics is a company dedicated to enhancing the quality of life of its customers by providing outstanding service and producing the highest quality products.

MAKING THE SOUND CHOICE

The decision to have a cochlear implant can be both exciting and a little confusing. The support and encouragement of family, friends or other cochlear implant users can be invaluable. There are several other resources available that may help in making this choice.

The best source of information is the cochlear implant center. Each implant center has audiologists, surgeons and other health care professionals who are specially trained in the field of cochlear implants. These individuals work as a team and will conduct a series of evaluations to determine if you are an implant candidate. Moreover, they will explain the benefits and limitations of cochlear implants and counsel you regarding your expectations. Advanced Bionics, the manufacturer of CLARION, works closely with each of its implant centers to ensure that they have the latest information about the CLARION device.

Additionally, organizations, such as Self Help for Hard of Hearing People (SHHH), Alexander Graham Bell Association for the Deaf (AGBell) and Cochlear Implant Club International (CICI) can provide general information as well as a list of other individuals who have cochlear implants.

Advanced Bionics recognizes the importance of the decision to obtain a cochlear implant and is available to answer any additional questions that may arise.

If you would like further information about CLARION or a listing of CLARION cochlear implant centers near you, please call or write Advanced Bionics Corporation.

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CLARION™ MULTI-STRATEGY™ COCHLEAR IMPLANT SYSTEM

PATIENT INFORMATION GUIDE FOR ADULTS

CAUTION: Federal law restricts this device to sale, distribution, and use by or on the order of a physician.

Authorized to affix the CE mark in 1993.

CE

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This guide is for adults who are considering a CLARION™ Multi-Strategy™ Cochlear Implant. It is designed to serve as a reference guide and instructional aid for learning about the CLARION system. While intended to answer basic questions, it is not a substitute for evaluation, training and counseling by a cochlear implant team. The cochlear implant team is the best source of information and can provide answers to any additional questions that you may have.

INTRODUCTION TO COCHLEAR IMPLANTS

A cochlear implant is an electronic device designed to provide useful hearing and improved communication ability to individuals who are profoundly hearing impaired and unable to achieve speech understanding with hearing aids. Hearing aids (and other types of assistive listening devices) make sounds louder and deliver the amplified sounds to the ear. However, for individuals with a profound hearing loss, even the most powerful of hearing aids may provide little to no benefit.

A profoundly deaf ear is typically one in which the sensory receptors, called the hair cells, of the inner ear are damaged. Making sounds louder or increasing the level of amplification does not enable such an ear to process sound. Cochlear implants bypass the damaged hair cells and stimulate the hearing nerves, allowing individuals who are profoundly or totally deaf to receive sound.

Cochlear implant technology was first researched and developed in the 1960s and 1970s. Since that time, cochlear implant systems have continued to improve from the first single-channel systems to the more recent multichannel devices. Today, advances in computer hardware and software and sound processing technology have produced implant systems that provide better sound than ever before.

Single channel devices were introduced in the 1970s. These early single electrode devices sent coded information to only one electrode site in the inner ear. These devices provided patients with speech and sound awareness and enhanced lipreading. Generally, speech understanding without lipreading was not achieved.

The introduction of multichannel devices in the 1980s represented a major advance in technology. Multichannel devices stimulate nerve fibers at multiple locations along the length of the cochlea and, thus, provide greater pitch discrimination. Stimulating nerve fibers at multiple locations is important because each nerve fiber in the inner ear is "tuned" to a different pitch depending on its location. Hearing nerves are organized so that high frequencies are picked up at the base of the cochlea while low frequencies are picked up at the center or apex. This arrangement is referred to as the "tonotopic" organization of the ear. With the introduction of multichannel systems, some cochlear implant recipients were able to understand speech without lipreading.

The latest advance in cochlear implant technology has been the development of multichannel systems that provide users with access to more than one speech processing strategy. Speech processing is the method by which sound is converted or "processed" into electrical signals that can be sent to the brain to be interpreted as sound. The ability of a cochlear implant system to allow patients to experience and use more than one speech processing strategy is referred to as multi-strategy.

CLARION is representative of these most recent developments in cochlear implant technology. It is a multichannel, multi-strategy device and incorporates some of the latest advances in computer technology and signal processing. It is the result of many years of extensive research and development at leading research institutions around the world.

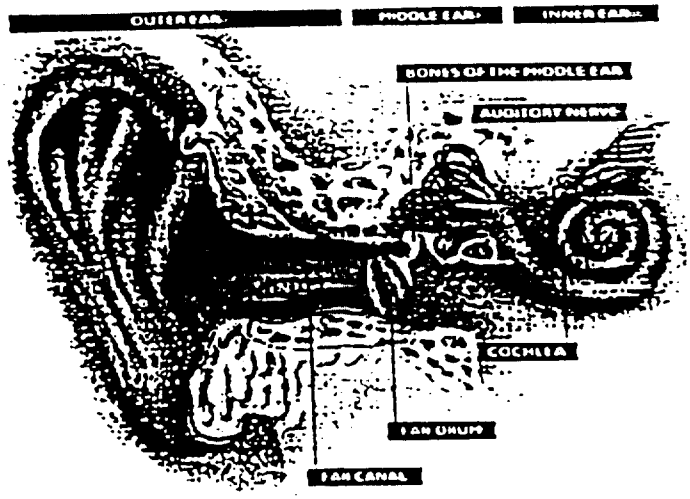
HOW THE EAR WORKS

In order to understand how a cochlear implant works, it is helpful to have a basic understanding of how the ear normally functions to process sound.

The ear is a remarkable mechanism which consists of three parts:

Outer ear: the visible outer portion of the ear and ear canal
Middle ear: the eardrum and three tiny bones
Inner ear: the fluid-filled, snail-shaped cochlea which contains thousands of tiny hair cells

When the ear functions normally, sound waves travel through the air to the outer ear which collects the sound and directs it through the ear canal to the middle ear. The sound waves strike the eardrum and cause it to vibrate. This vibration creates a chain reaction in the three tiny bones in the middle ear. Motion of these bones generates movement of the fluid contained in the snail shaped inner ear, known as the cochlea. The cochlea is lined with thousands of tiny hair cells. As the fluid in the cochlea begins to move, the hair cells convert these mechanical vibrations into electrical impulses and send these signals to the hearing nerves. The electrical energy generated in the hearing nerves is sent along the auditory nerve to the brain where these signals are interpreted as sound.



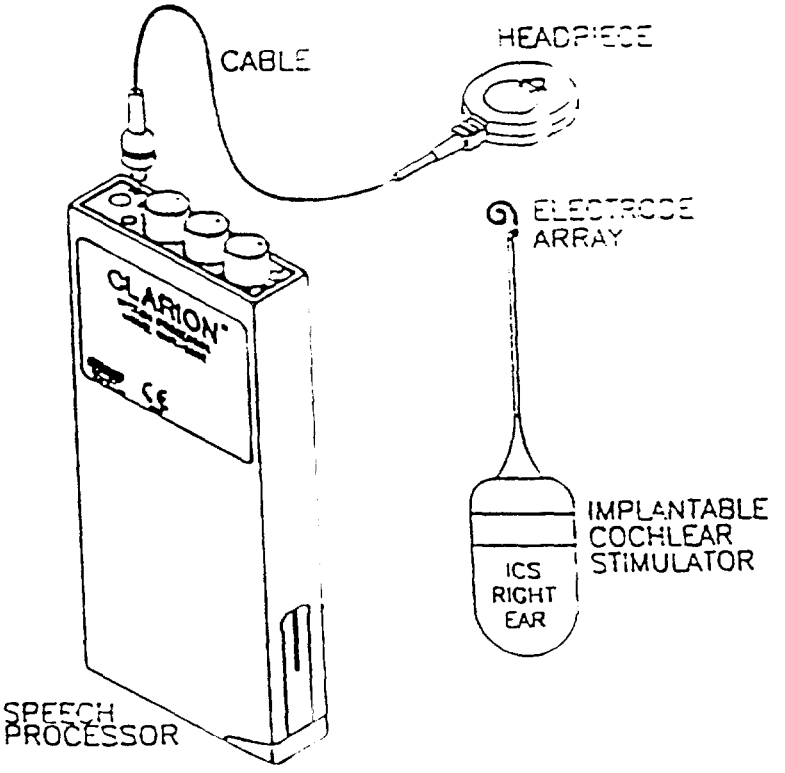
In many individuals with a profound hearing loss, the hair cells may be damaged or depleted. In these cases, electrical impulses cannot be generated. Without these electrical impulses, the hearing nerves cannot carry messages to the brain. Even the loudest of sounds may not be heard. Although the hair cells in the cochlea may be damaged, there are usually some surviving hearing nerve fibers. A cochlear implant works to bypass the damaged hair cells and stimulate the surviving hearing nerve fibers with an electrical signal. The stimulated nerve fibers then carry the electrical signals to the brain.

CLARION MULTI-STRATEGY COCHLEAR IMPLANT

CLARION is a new generation cochlear implant and incorporates some of the latest advances in electronic circuitry, computer hardware and software, and speech processing technology.

CLARION System Components

CLARION consists of both internal and external components. The internal components are those parts of the system that are surgically implanted under the skin behind the ear, and are referred to as the **implantable cochlear stimulator (ICS)**. The external components include the **speech processor**, which is usually carried on a belt or in a pocket, and a **cable and headpiece**, which is worn on the head just behind the ear. Additionally, there are accessory items, such as an auxiliary microphone, telephone pick-up coil and a carrying case. The figure below shows the major components of the CLARION system.



The **ICS** includes the electronics of the implant, referred to as a receiver/stimulator, a magnet and a curved electrode array. It is made of materials that have been thoroughly tested for compatibility with the body and for durability. The receiver and magnet are fully encased in a sealed ceramic case. The receiver accepts and decodes signals from the external components of the system and conveys these signals to the electrode array in the cochlea.

The electrode array extends from the ceramic case and is designed to be inserted approximately 24 millimeters or one inch into the cochlea. The electrode array consists of 16 electrodes arranged in 8 staggered pairs to allow for stimulation of discrete segments along the cochlea, thereby allowing detailed pitch discrimination.

The **speech processor** is a powerful microcomputer that converts incoming sound into distinct electrical code. The conversion of sound into code is accomplished through software programs, called speech processing strategies. The speech processor has adjustable controls, such as volume and sensitivity. The volume and sensitivity controls can be set according to the needs of the user and the listening environment.

The speech processor is powered by a rechargeable battery pack. Two battery chargers and six rechargeable battery packs are provided with every CLARION system. A fully charged battery provides an average of 9 hours of continuous use.

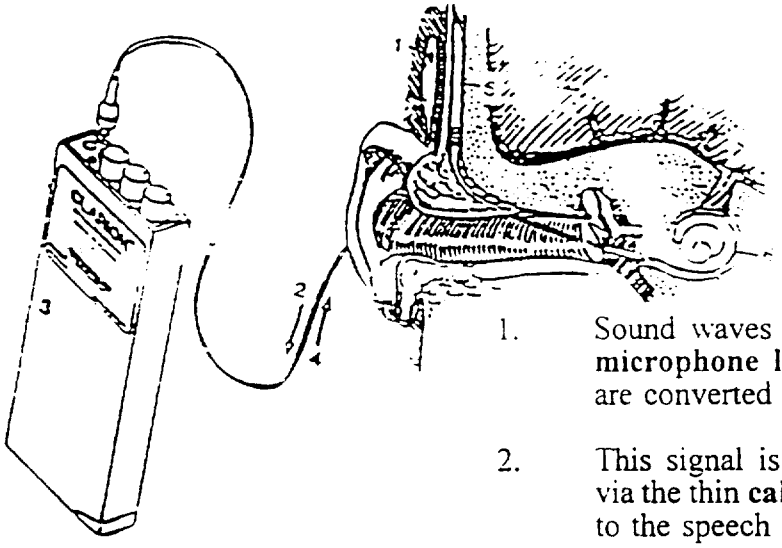
The **headpiece** is held in place by a magnet that aligns with the magnet in the implanted device. It contains a microphone which picks up sounds from the environment and sends them to the speech processor via a thin **cable** that connects the headpiece to the speech processor.

In addition to the microphone in the headpiece, CLARION comes with an additional auxiliary microphone which can be placed in various locations according to individual preference.

Detailed information regarding the external components of the CLARION system and instructions for use are contained in the CLARION *User's Handbook*.

How CLARION Works to Produce Sound

CLARION converts sounds in the environment into electrical code and sends this code to the hearing nerves. Below is a step-by-step outline of the way CLARION works. Each numbered step corresponds to a number indicated in the illustration below:



1. Sound waves enter the system through the **microphone located in the headpiece** and are converted into an electrical signal.

2. This signal is sent to the speech processor via the thin **cable** that connects the headpiece to the speech processor.

3. The **speech processor** converts the electrical signal into a distinctive code that has been determined to be the most useful for sound and speech understanding. The translation of sound into code is accomplished through software programs, called speech processing strategies.

4. Once processed, the electrically coded signal is sent back up the **cable** to the headpiece and transmitted across the skin via radio waves to the implanted device.

5. The **implanted device** decodes the signal and delivers it to the array of electrodes positioned within the cochlea.

6. The **electrodes** bypass the hair cells and stimulate the auditory nerve fibers within the cochlea. Each electrode is adjusted to suit the loudness range of the individual and programmed to receive differently processed signals. Depending on the particular signal being transmitted, specific electrodes are stimulated and, in turn, stimulate particular segments of the hearing nerves.

7. Stimulation of the hearing nerves causes electrical impulses to be delivered to the brain where they are interpreted as sound. The entire process–from incoming sound to processing in the brain–occurs so rapidly that the user hears sound as it happens.

Features of CLARION

Choice of Speech Processing Strategies Today...

Speech processing is the method by which incoming sound is converted or 'processed' into a special electrical signal which is then interpreted by the brain. CLARION offers users a choice of two different speech processing strategies that can be programmed into the same speech processor at the same time. One strategy converts sound into digital pulses and delivers these pulses to the electrodes very rapidly in sequence. This strategy is referred to as the Continuous Interleaved Sampler (CIS) strategy. The other strategy converts sound into analog waveforms and stimulates all of the electrodes at the same time. This strategy is called the Compressed Analog (CA) strategy. The user can choose the strategy that provides the best sound or switch between strategies to maximize hearing.

...and Tomorrow

Speech processing strategies are actually computer software programs. CLARION is designed to incorporate new software programs similar to the way software programs are added to a computer. There is no need for additional surgery or to replace expensive hardware with each new advance in speech processing technology. However, just as with computers, as cochlear implant technology continues to advance, it is possible that existing equipment would need to be replaced in order to take advantage of these changes.

Detailed Representation of Speech Sounds

CLARION processes and sends information to the inner ear at a high rate of speed, which delivers a detailed representation of speech sounds. The CLARION speech processor contains a powerful microcomputer chip which is capable of transmitting up to 104,000 pieces of information per second.

Engineered for Safety

CLARION incorporates many features to maximize safety. CLARION allows testing of the implanted device during the surgical procedure and at any time after surgery. This feature assures the patient and physician that all components of the implant are functioning properly. The implant electronics include special components, called capacitive couplers, to prevent the leakage of direct current which could damage internal tissues. Additionally, both CLARION's internal electronics and the receiving coil are sealed within a durable ceramic case to prevent breakage.

Engineered for Reliability

CLARION is manufactured by Advanced Bionics Corporation, a company dedicated to providing the highest quality products and services. Advanced Bionics is a spin-off from the second largest pacemaker manufacturer in the world.

CANDIDATES FOR CLARION–ADULTS

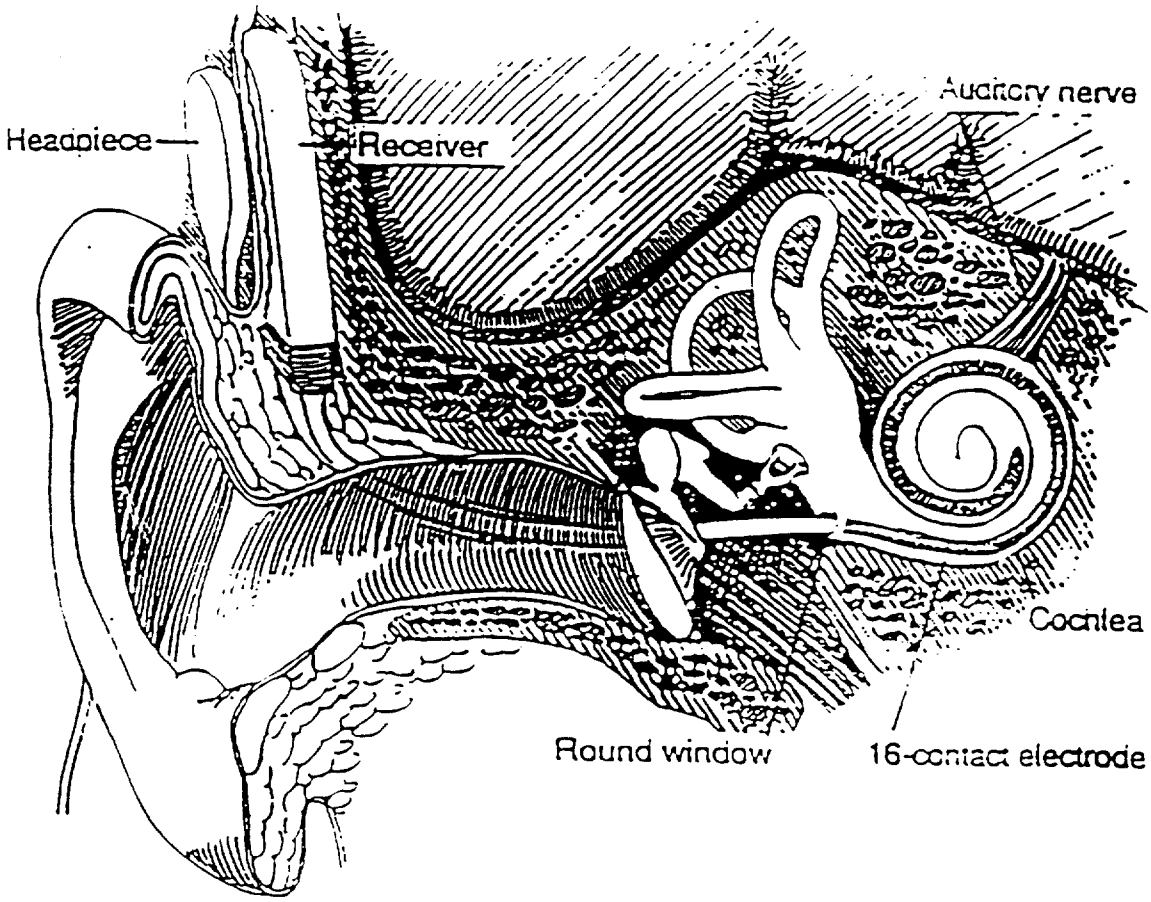
Your physician and the implant team can determine if CLARION is right for you. CLARION is indicated for use in adults, 18 years of age or older, with a profound, sensorineural hearing loss in both ears (90 decibels or greater). Normal speech and conversation usually occur at 50 to 60 decibels. The term sensorineural applies to individuals with "nerve deafness." Candidates should be unable to understand speech through the use of appropriately fitted hearing aids, and have lost their hearing after some speech and language skills have been learned. In addition, candidates should be in good health and motivated to learn to hear again.

In order to determine if an individual is a candidate for CLARION, a complete hearing (audiological) evaluation is conducted by the implant center. This evaluation will assess the candidate's type of hearing impairment, level of hearing loss and performance with appropriately fitted hearing aids.

In addition to an audiological assessment, the selection process includes various medical tests such as an ear examination and x-rays of the cochlea. These tests are performed to verify that there is no external or middle ear disease that might prevent implantation. Specific conditions may prevent a person from qualifying for the implant. For example, bony growth (ossification) of the cochlea may disqualify an individual because ossification may prohibit full insertion of the electrode. Also, individuals with deafness due to lesions of the acoustic nerve or with an absence of cochlear development are not candidates. In addition to the tests used to determine if an individual is a candidate for a cochlear implant, other medical tests may be conducted to ensure that an individual is able to undergo surgery without risks to general health.

SURGICAL PROCEDURE

The purpose of the surgical procedure is to implant the internal components of the system, consisting of the electrode array and the electronic receiver. The receiver is placed under the skin and behind the ear on the mastoid bone. The electrode array is inserted into the cochlea through the round window, for a distance of about 24 millimeters or approximately one and a half turns of the cochlea. The figure below shows an ear with the implanted components in place.



The surgery is done under general anesthesia and generally takes between two and three hours. The procedure can be performed in either the inpatient or outpatient setting. Immediately before surgery, the small area behind and above the ear to be implanted is shaved to reduce the possibility of infection near the implant site. The hair grows back naturally over this area.

The procedure begins with an incision behind and above the ear that allows access to the cochlea and to the mastoid area. The incision must be sufficiently large so that the receiver and electrode array can be placed without any portion touching the line of incision. This reduces the possibility of infection. After the appropriate preparations, the electrode array is carefully positioned in the cochlea, the receiver is placed in a surgically created depression on the mastoid bone, and the incision is closed with stitches or staples.

Patients are usually able to get out of bed and walk around their room the day after surgery and generally are discharged from the hospital on the first postoperative day. The sutures are removed from the incision approximately seven days after surgery.

Following release from the hospital, patients return home for a period of four to six weeks. This allows for a complete recovery period, although patients generally report that they are at "full-strength" and "back to normal" within a week or two after the surgery. The four to six week recovery period permits complete healing around the implant site before the patient returns to the clinic to be fitted with the external components of the system.

The risks of surgery and cochlear implantation will be fully discussed with you by your implant team.

DEVICE FITTING

After the healing period, patients return to the implant center to begin the process of "fitting" the external portion of the system. This procedure is preformed by an audiologist who works as part of the implant team. The fitting process involves programming the device to meet each person's individual needs. An interactive, computerized program guides the patient and audiologist through the fitting process. The audiologist and patient work together to find the processor settings that provide the best sound information. Because alternative techniques for programming the processor are available, the device fitting procedure varies in time for each individual. The audiologist may want to fit an individual with two different processing strategies to find the one that yields the best results. The initial device fitting typically takes a few hours and may be done in one or more sessions.

Initial Fitting Process

Initially, sounds or tones are presented to each electrode or electrode pair (channel) until the individual is able to detect the sound and an appropriate comfort level is determined. This process is performed channel by channel and may use two different waveforms (pulsatile and analog) in order to establish the basic settings needed to test and compare the two alternative speech coding schemes. Once the basic settings are known, the speech processor is programmed to send the specified signals to the electrodes. This group of tests is generally referred to as psychophysical measures.

Using the psychophysical information, speech sounds are then presented so that a comfort level for speech is established. This may be done with the processor configured in two different ways so that results with two different speech processing strategies can be compared. Finally, using either live voice or recorded speech materials, the patient will have an opportunity to compare the sound of ongoing conversational speech with two different processing schemes.

In addition to the formal device fitting process, the audiologist will discuss any impressions and sensations that may be experienced. Input regarding the clarity and quality of speech that is heard is a very important element of the device fitting process. Based on both test results and feedback regarding what sounds best, the speech processor will be programmed with one or two speech processing strategies. In this way, individuals will be able to experiment and try different processing schemes in familiar environments.

CLARION gives the audiologist the opportunity to program two different speech processing strategies into one speech processor. Both strategies can be programmed into the speech processor at the same time. Users can listen to sound with the different strategies and determine which strategy they like best. Some individuals prefer one strategy, some prefer another, and others switch between the two strategies depending on the listening environment. The audiologist will work with each individual to determine the most effective strategy or strategies.

In addition to device fitting, time will be devoted to training the user on the use and care of the CLARION system. Discussions may include correct positioning of the headpiece, battery pack insertion, and use of the adjustable patient controls. Troubleshooting is also discussed. A complete discussion of how to use the speech processor is contained in the CLARION *User Handbook.*

Follow-up Visits

During the first several months of device use, users may be seen on several occasions for readjustment of the speech strategies programmed into the speech processor. Thereafter, follow-up visits typically occur on a six-month or annual basis. Methods of promoting maximum use of the new sounds being heard, as well as development of lipreading and other communication skills, may also be explored.

BENEFITS OF CLARION

The benefits of CLARION were demonstrated in an extensive clinical study of postlingually deafened (≥90 dB) adults who were consecutively implanted with CLARION at leading implant centers across the United States. Clinical results were reported on the number and percentage of patients demonstrating statistically significant improvement and achieving a particular level of performance. The study subjects were tested in quiet at normal conversational levels (50 - 55 dB) at six months of device usage. All improvement results are based on comparisons to pre-implant data in the best aided condition.

Clinical Study Results

- All subjects (100%) detected speech and sounds at comfortable listening levels. (68 subjects tested)

- Fifteen subjects (28%) demonstrated improvement in the recognition of familiar warning signals. Preoperatively with hearing aids, 23 subjects (43%) identified half or more of familiar warning signals. Postoperatively with the implant, 47 subjects (89%) identified half or more of familiar warning signals. (53 subjects tested)

- Fifty-eight subjects (87%) improved their communication ability when the device was used in conjunction with lipreading. Fifty-six subjects (84%) achieved scores over 50% on sentences* with lipreading. Forty-nine subjects (73%) achieved scores over 75% on sentences* with lipreading. Thirty-four subjects (51%) achieved scores over 90% on sentences* with lipreading. (67 subjects tested)

  *CUNY Sentences, representing standard everyday speech, presented via laser disk and requiring exact repetition.

- Fifty subjects (74%) demonstrated improvement in open-set sentence recognition without lipreading compared to aided pre-implant performance. Fifty-one subjects (75%) achieved scores over 20% on sentences* without lipreading. Thirty-five subjects (51%) achieved scores over 80% on sentences* without lipreading. Seventeen subjects (25%) achieved scores over 95% on sentences* without lipreading. Seventeen subjects (25%) scored less than 20% on sentences* without lipreading. (68 subjects tested)

  *CID Sentences, representing standard everyday speech, presented via monitored audio tape recordings and requiring recognition of key words.

- Forty-seven subjects (69%) demonstrated improvement in open-set monosyllabic word recognition without lipreading compared to aided pre-implant performance. Thirty-four subjects (50%) achieved scores of 30% or greater on monosyllabic words* without lipreading. Twenty-three subjects (34%) achieved scores over 45% on monosyllabic words* without lipreading. Eighteen subjects (26%) achieved scores of 50% or greater on monosyllabic words* without lipreading. (68 subjects tested)

  *NU-6 Words, representing single syllable words, presented via monitored audio tape recordings and requiring exact repetition.

- Forty-three subjects (64%) demonstrated improvement in open-set sentence recognition. over the telephone compared to aided pre-implant performance. Thirty-six subjects (54%) achieved scores over 65% on sentences* heard over the telephone. Twenty-seven subjects (40%) achieved scores over 80% on sentences* heard over the telephone. Eighteen subjects (27%) achieved scores over 95% on sentences* heard over the telephone. (67 subjects tested)

  *Overlearned Sentences, representing previously unknown, familiar phrases, presented over the telephone and requiring recognition of key words.

- Fifty-one subjects (75%) self-assessed their ability to communicate without lipreading as improved compared to aided pre-implant performance. Fifty-eight subjects (85%) self-assessed their ability to communicate with lipreading as improved compared to aided pre-implant performance. (68 subjects tested)

ADVERSE EVENTS, WARNINGS AND PRECAUTIONS

Adverse events, warnings and precautions of cochlear implantation will be fully explained to the implant candidate by the surgeon and audiologist. Cochlear implantation procedures have been performed for over 15 years and are considered safe.

Adverse Events

Safety data are based on a total of 273 patients who were implanted during the clinical study (148 U.S. patients and 125 international patients) of CLARION. Not all subjects were evaluated for all effects. For example, 46 U.S. patients participated in a 12-month postoperative questionnaire and 98 U.S. patients were evaluated for symptoms of dizziness. The following adverse events occurred during the clinical trial using CLARION.

- For all patients, implantation of the cochlear implant resulted in a palpable lump behind the ear.
- For all patients, insertion of the intracochlear electrode array resulted in the loss of residual hearing in the ear that was implanted.
- Five patients experienced device migration (movement), one patient experienced device extrusion, and two patients experienced device exposure. These problems were due to improper surgical placement of the implant.
- Three patients experienced electrode displacement (one case of full displacement and two cases of partial displacement) due to improper use of the electrode insertion tool.
- Four patients experienced facial nerve stimulation. All cases of facial nerve stimulation were resolved through reprogramming of the device.
- Two patients experienced electronic device failures and required surgery to replace the device.
- Ninety-eight patients were evaluated for preoperative and postoperative vestibular symptoms. Follow-up time varied from six to 24 months. Of the 83 patients who reported no preoperative vestibular symptoms, 26 patients reported mild, fluctuating dizziness postoperatively. None of the cases of postoperative dizziness required medical intervention.
- Forty-six patients participated in filling out a tinnitus questionnaire at the 12 month postoperative follow-up. Four patients who reported experiencing no tinnitus prior to surgery reported tinnitus with the implant turned both on and off. Twenty-two patients who reported experiencing tinnitus prior to surgery reported no tinnitus postoperatively with the implant turned on.
- One patient experienced an inability to achieve magnetic adherence between the headpiece and the implant which was resolved by a surgical thinning of the flap over the implant.
- One patient experienced skin irritation over the implant.

Possibe Adverse Events

Although there were no reports during the clinical study of the following adverse events. these additional events are known to be possible adverse events associated with cochlear implants.

- Implant patients will incur the normal risks of surgery and general anesthesia.
- Major ear surgery may result in numbness. swelling or discomfort about the ear. disturbance of taste or balance. or neck pain. If these occur. they are usually temporary and subside within a few weeks of surgery.
- Rarely, cochlear implantation may cause a leak of the inner ear fluid which may result in meningitis.
- Implantation of the internal device may cause infection that can usually be treated with conventional antibiotics. but in some instances may require removal of the device.

Warnings

- **Electrosurgical instruments** must not be used within the vicinity of a cochlear implant and/or its electrode system. Electrosurgical instruments are capable of producing radio frequency voltages of such magnitude that a direct coupling can effectively exist between the cautery tip and an electrode array. Induced currents could cause damage to the cochlear tissues or permanent damage to the implant.
- **Diathermy** must never be applied over the receiver/stimulator or electrode lead of the cochlear implant. High currents induced into the electrode lead can cause tissue damage to the cochlea or permanent damage to the implant.
- **Electroconvulsive therapy** must never be used on a cochlear implant patient. Electroconvulsive therapy may cause tissue damage to the cochlea or permanent damage to the implant.
- **Ionizing Radiation Therapy** cannot be used directly over the cochlear implant as it may damage the device.
- Exposure of the cochlear implant to a **Magnetic Resonance Imaging (MRI)** device may cause deleterious effects to the implant and to the patient. Individuals with a CLARION cochlear implant cannot undergo an MRI procedure or be in the same room with an MRI system, regardless of whether the system is in operation or not. The inability to undergo an MRI procedure prevents access to an important diagnostic modality.

  The effects of **cobalt treatment and linear acceleration** techniques on the implant are unknown.
- **Insertion of an intracochlear electrode** will result in the loss of any residual hearing in the implanted ear.
- The long term effects of **chronic electrical stimulation** are unknown. Such effects may include new bone growth in the cochlea or deterioration of the auditory nerves. These effects may preclude replacement of the electrode array or lead to deterioration of the cochlear response.

- **Electrode displacement** can occur if the electrode is not inserted properly. Surgeons should be proficient in the use of the electrode insertion tool.

- **Extrusion or migration of the implant** can occur if the device is not properly recessed into the mastoid bone. Surgeons should be skilled in the recommended surgical technique to implant CLARION

- **Extreme direct pressure** on the implanted device, up, down, left or right may cause the implant to move and possibly dislodge the electrode array. The implanted device is surgically placed on the mastoid bone and is capable of withstanding the effects of running, exercise and normal activity. A direct hit by a hard object or sharp blow to the implant may damage the device. It is recommended that individuals participating in any type of contact sports wear a helmet or protective headgear. The surgeon or audiologist should be called if is suspected that the device has been damaged.

Precautions

- **Static electricity** has the potential of damaging the electrical components of a cochlear implant system. Care should be taken to avoid situations in which static electricity is commonly created, such as when pulling on and off clothes or walking across a wool rug. If static electricity is present, patients should touch something conductive (e.g., a metal object) before their cochlear implant device contacts another person or object.

- **Airport or security metal detectors** may be activated by the cochlear implant system; thus, it is advised that patients carry their "Patient Emergency Identification" card with them at all times.

- Cochlear implants do not restore normal hearing and benefits vary from one individual to another. Benefits range from the recognition of speech and sounds at comfortable listening levels to speech understanding with and without lipreading and over the telephone. There appears to be little correlation between the degree of benefit obtained from an implant and the cause of deafness.

- There are no definitive tests which can be administered prior to implantation that estimate the degree of benefit an individual may receive. Not all patients will achieve at least 20% on tests of open-set sentence recognition without lipreading (i.e., CID Sentences) with the implant. (Refer to Clinical Study Results)

- Implant recipients should only use the speech processor that has been specifically programmed by the clinician for them. Use of a different speech processor may be ineffective in providing sound information and may cause physical discomfort from overstimulation.

FREQUENTLY ASKED QUESTIONS

The following section has been written to provide answers to some of the most commonly asked questions about cochlear implants.

How long have cochlear implants been used?

Experimentation with electrical stimulation was first done by French researchers in the late 1950s. Since then, cochlear implants have been in development around the world.

How much does a cochlear implant cost and will insurance pay for it?

As with most medical prostheses, cochlear implants are expensive. Many insurance carriers provide full or partial coverage for cochlear implants and the associated costs. The amount of coverage depends on the specific insurance carrier. The implant center submits the proper documentation to the insurance carrier for approval. Additionally, reimbursement assistance is available for CLARION from the insurance reimbursement department at Advanced Bionics. The insurance department will work with the individual, the implant center and the insurance company to help implant candidates receive the maximum coverage available through their insurance carriers.

Are there any restrictions on physical activities?

The implanted device is capable of withstanding the effects of running, exercise and normal activity. However, precautions must be taken when participating in contact sports in order to avoid any blows to the head. Additionally, the external components of the system should be protected from moisture and breakage. The speech processor and headpiece must be removed before bathing or swimming or when participating in an activity where these components could get wet.

Is CLARION covered under warranty?

CLARION is designed to withstand the wear and tear of daily life. The implanted components are warranted for five years, while the speech processor has a three-year warranty. Over time, the batteries and cables may need to be replaced. When first receiving the system, spare batteries, cables and accessory equipment are provided.

Who developed and designed CLARION?

CLARION is the result of many years of extensive research and development and represents the cooperative efforts of the University of California, San Francisco (UCSF), Research Triangle Institute (RTI), the A.E. Mann Foundation for Scientific Research and the device manufacturer, Advanced Bionics Corporation.

For over twenty years, UCSF has been engaged in cochlear implant research and development. Research has focused on the design and production of a cochlear implant capable of differentially stimulating small regions of the auditory nerve. UCSF designed and developed the unique electrode array used with CLARION. Research at RTI has focused on the development of speech processing strategies for auditory prostheses and is recognized as a world leader in the modeling of the electrically-stimulated cochlea. Through their joint investigations, UCSF and RTI have demonstrated that each implant recipient may not be suited to the same speech processing strategy and that gains in speech recognition can be made by selecting the best type of processing for the individual patient. Advanced Bionics, the device manufacturer, has long been associated with the development and production of implantable devices requiring technological advances in hermetic packaging, integrated circuits, and signal processing.

Will CLARION ever need replacing?

The implanted device is designed to last a lifetime. The materials used in its construction are fully biocompatible and durable. However, despite extremely cautious and careful quality control and inspection, a device failure could occur. Because of the implant's unique telemetry feedback system, an internal device problem can be detected externally. In such an instance, it may be necessary to remove and replace the device.

CLARION is a state-of-the-art system and incorporates advanced techniques of signal processing and the most recent concepts in speech processing. Through its flexibility and transmission capabilities, it is designed to take advantage of and adapt to future speech processing strategies that may yield greater speech understanding. Speech processing strategies are actually computer software programs. CLARION is designed to incorporate new software programs similar to the way software programs are added to a computer. Thus, individuals implanted now may be able to benefit from future research without having to undergo a surgical replacement of the device. However, just as with computers, as cochlear implant technology continues to advance, it is possible that the speech processor may need to be replaced in order to take advantage of these future changes.

What is Advanced Bionics' commitment to the field of cochlear implants?

Advanced Bionics is a spin-off from the second largest heart pacemaker manufacturer in the world. CLARION represents years of extensive research and development and the collaborative efforts of the some of the world's leading research institutions in the field of cochlear implants. Ongoing research continues and Advanced Bionics is committed to maintaining its position at the forefront of new technology and development.

Advanced Bionics is a company dedicated to enhancing the quality of life of its customers by providing outstanding service and producing the highest quality products.

What advances can be expected in the field of cochlear implants?

Several advances are anticipated in the future development of cochlear implants. Improvements are expected in the ability of the implant to provide better speech understanding as new speech processing strategies are developed. At several implant centers around the world, research is continuing on methods for estimating and mapping the location and magnitude of surviving auditory nerves. Once the pattern of nerve survival is known, the possibilities for providing individuals with a speech processing scheme optimally matched to the individual are greatly increased. Further miniaturization of the external components of devices is probable, with the promise of far smaller and lighter devices in the future. Thus, individuals currently implanted with the CLARION system may be able to take advantage of and benefit from ongoing implant research without requiring surgical replacement of implanted components.

CONCLUSIONS

The decision to have a cochlear implant is a major one. There are several resources available that may help in making this choice. The most valuable source of information is the cochlear implant center. Each implant center has professionals, audiologists and surgeons specially trained in the field of cochlear implants. These individuals work as a team and will conduct an evaluation to determine implant candidacy. Moreover, they will explain the benefits and limitations of cochlear implants and counsel individuals regarding their expectations. Advanced Bionics, the manufacturer of CLARION, works closely with each of its implant centers to ensure that they have the latest information about CLARION. Additionally, the staff at Advanced Bionics is available to assist in providing information and service.

Organizations, such as Self Help for Hard of Hearing People (SHHH), Cochlear Implant Club International (CICI) and the Alexander Graham Bell Association for the Deaf (AGBell) can provide general information about cochlear implants and put candidates in touch with other cochlear implant recipients. Most importantly, however, may be the support of family and friends. Their support during the decision making process, surgery, fitting and adjustment to hearing through the cochlear implant can be invaluable.

If you are interested in learning more about cochlear implants or in locating a CLARION cochlear implant center near you, please call or write Advanced Bionics Corporation.

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