# SUMMARY OF SAFETY AND EFFECTIVENESS

## I. General Information

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|---|---|
| A. Device Generic Name: | Implantable Middle Ear Hearing Device |
| B. Device Trade Name: | Vibrant® P Soundbridge™, consisting of:<br>Vibrating Ossicular Prosthesis™ (VORP™) [Model 502]<br>Audio Processor™ [Model 302]<br>Programmer [Model 600]<br>Surgical Accessory Kit<br>Audio Processor Fitting Kit<br><br>Vibrant® D Soundbridge™, consisting of:<br>Vibrating Ossicular Prosthesis™ (VORP™) [Model 502]<br>Audio Processor™ [Model 304]<br>Programmer [Model 700]<br>Surgical Accessory Kit<br>Audio Processor Fitting Kit |
| C. Applicant's Name and Address: | Symphonix Devices, Incorporated<br>2331 Zanker Road<br>San Jose, California 95131 |
| D. Premarket Approval (PMA) Application Number: | P990052 |
| E. Date of Panel Meeting:<br>Panel Recommendation: | July 20, 2000<br>Approvable with Conditions |
| F. Date of GMP Clearance and Final Approval: | August 24, 2000 |
| G. Date of Notice of Approval to Applicant: | August 31, 2000 |

## II. Indications for Use

The Vibrant Soundbridge System, hereinafter referred to as the Vibrant Soundbridge, is an implantable middle ear hearing device intended to provide a useful level of sound perception to individuals via mechanical stimulation of the ossicles. The Vibrant Soundbridge is intended for use in adults, 18 years of age or older, who have a moderate to severe sensorineural hearing loss and desire an alternative to an acoustic hearing aid. Prior to receiving the device, it is recommended that an individual have experience with appropriately fit hearing aids.

## III. Device Description

The Vibrant Soundbridge consists of two main subsystems: 1) the implant (called the Vibrating Ossicular Prosthesis or VORP); and 2) the external amplification system (called the Audio Processor).

The VORP consists of three (3) functional components:

1. *Implanted receiver unit:* The implanted receiver unit receives the electromagnetic signal from the external amplification system. A demodulator circuit filters the modulated signal to the appropriate drive signal for the transducer.
2. *Conductor link:* The conductor link is the electrical conduit that connects the transducer to the implanted receiver unit.
3. *Floating Mass Transducer™:* The Floating Mass Transducer drives the middle ear bones in response to sound. It is very small, approximately 2 mm in length by 1.5 mm in diameter.

The Audio Processor consists of four (4) functional components:

1. *Microphone*: The microphone picks up sound from the environment and delivers a corresponding electronic signal to the sound processing system.
2. *Sound processing system:* The sound processing system modifies the signal output to the patient's specific requirements for her or his hearing loss and dynamic range. The sound processing circuitry is programmable with an external, hand-held programmer. The sound processing circuitry can be controlled in defined frequency bands. The gain can be controlled in each band as well as the crossover frequency, the threshold knee, and the output volume.
3. *Modulator circuit:* This circuit modulates the signal frequency of the output of the signal processor. The reason for signal modulation between the external amplification system and the internal implant unit is to reduce potential noise interference from broad band electromagnetic fields.
4. *Battery:* A battery powers the device. Since the device is based on standard hearing aid signal processing technology, a standard (1.5-volt) hearing aid battery is used.

The size of the Audio Processor is approximately 1.2 inches in diameter and is designed to be worn under the hair, behind or above the external ear. There are two versions of the Audio Processor: the Model 302 Audio Processor (Vibrant P Soundbridge) and the Model 304 Audio Processor (Vibrant D Soundbridge).

The Programmer consists of three (3) functional components:

1. *Programming Unit:* The programming unit allows the audiologist to modify various signal processing parameters of the Audio Processor in accordance with a patient's individual hearing requirements.
2. *Programming Cable:* A programming cable connects the Programmer to the Audio Processor.
3. *Battery:* The Programmer is battery powered. There are no mains supply or charging requirements.

There are two versions of the Programmer: the Model 600 Programmer for use with the Model 302 Audio Processor (Vibrant P Soundbridge) and the Model 700 Programmer for use with the Model 304 Audio Processor (Vibrant D Soundbridge).

A surgical accessory kit, audiologist's fitting kit, and Audio Processor Adapter™ are also part of the system. The Audio Processor Adapter permits an audiologist to qualitatively assess the functionality of an Audio Processor without patient involvement.

## IV. Contraindications and Warnings

Please refer to approved labeling.

## V. Alternative Practices and Procedures

The alternative practices and procedures available to Vibrant Soundbridge users include acoustic hearing aids. Hearing aids can be worn in a variety of styles including behind-the-ear, in-the-ear, or completely-in-the-canal.

## VI. Marketing History

The Vibrant P Soundbridge was authorized to bear the CE mark on March 6, 1998. The Vibrant D Soundbridge was authorized to bear the CE mark on May 19, 1999. Since market introduction and as of July 31, 2000, Symphonix Devices, Inc. has commercially distributed approximately 205 Vibrant Soundbridges throughout the European Union and Switzerland. The devices have not been withdrawn from any market for any reasons related to safety or effectiveness.

## VII. Potential Adverse Effects of the Device on Health

Potential adverse effects on health associated with implantable middle ear hearing devices include a decrease in residual hearing and the normal risks of surgery such as infection in the ear and adjacent structures and general anesthesia. Major ear surgery may result in numbness, swelling, or discomfort around the ear, the possibility of facial paresis, disturbance of balance or taste, or neck pain.

## VIII. Summary of Preclinical Studies

The objective of the preclinical studies was to provide reasonable assurance of the safety of the Vibrant Soundbridge prior to clinical testing. In addition, the sponsor provided a Declaration of Conformity to the following recognized consensus standards:

- ANIS/AAMI/ISO 10993-1 Biological Evaluation for Medical Devices, Part 1, Evaluation and Testing.

  Audio Processor – The molded plastic material used in the Audio Processor P (Model 302) and the Model Audio Processor D (Model 304) was tested in accordance with the applicable subsections of the standard for *Device Category: Surface Devices, Skin Contact, Contact Duration :C (Permanent, >30 days).*

  Deviations: As permitted by the study protocol, the test material was molded as the bottom case component of an Audio Processor, and represented the same material, processing, and handling of finished Audio Processors. This deviation has no effect on the test results reported.

  Vibrating Ossicular Prosthesis – The Vibrating Ossicular Prosthesis (Model 502) was tested in accordance with the applicable subsection of the standard *for Device Category: Implant Device, Tissue/Bone Contact, Contact Duration: C* (permanent *>30 days).*

  Deviations: As permitted by the study protocol, the test samples were non-functional units. The internal magnet component and demodulation electronics components were substituted with titanium mock-ups representing the same material and form factor as actual production components. The test samples were otherwise manufactured in accordance with the identical materials, components, processing and handling, including sterilization, as that of the finished devices. This deviation has no effect on the test results.

- AAMI 10993-7:1995 Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals
- AAMI 11135:1994 Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization
- ISO 11737-1:1995 Sterilization of Medical Devices-Microbiological Methods – Part 1: Estimation of the Population of Microorganisms on Product

Deviations: As permitted by the study protocol, the samples used in the half-cycle and fractional cycle portions of the testing were facsimile VORPs. That is, the samples did not contain functional electronics. The samples were built in a manner identical to that of the device intended for marketing. The samples have the identical exterior molded silicone elastomer and medical grade epoxy as that of the device intended for marketing. This deviation has no effect on the test results reported.

A. Biocompatibility Testing

1. Vibrating Ossicular Prosthesis (VORP Model 502)

A series of *in vitro* and *in vivo* studies were conducted on the medical grade silicone elastomer and the medical grade epoxy components of the VORP implant contacting tissue to demonstrate that the materials were biocompatible. All testing was conducted in conformance with 21 C.F.R. § 58 – *Good Laboratory Practice for Nonclinical Laboratory Studies.*

The titanium, gold wire, and polyimide-coated gold wire incorporated in the VORP are not in body contact and are overmolded with silicone elastomer.

The materials were tested in finished form and passed the following tests: Cytotoxicity Test, Sensitization Test, Irritation Test, Acute Systemic Toxicity Test, Genotoxicity Tests, and Subcutaneous Implantation Tests.

2. Audio Processor (Model 302 and Model 304)

A series of *in vitro* and *in vivo* studies were conducted on the medical grade polycarbonate and medical grade silicone elastomer components of the Audio Processor contacting tissue to demonstrate that the materials were biocompatible. All testing was conducted in conformance with 21 C.F.R. § 58 – *Good Laboratory Practice for Nonclinical Laboratory Studies.*

The polycarbonate material was tested in finished form and passed the following tests: Cytotoxicity Test, Sensitization Test, and Irritation Test.

The test results raise no acute toxicological concerns and support the safety of the Vibrant Soundbridge for its intended use.

B. Animal Testing

*In vivo* studies were conducted using a calf model in conformance with 21 C.F.R. § 58 – *Good Laboratory Practice for Nonclinical Laboratory Studies.* Bull calves less than one month old were selected as the model of choice due to similarities in the mass and the size of the calves' ossicles to that of human ossicles. Five (5) bull calves were implanted with the Floating Mass Transducer (FMT). The sixth bull served as a sham control. Sound thresholds to clicks and tone bursts of the Auditory Brainstem Response (ABR) were monitored for eight (8) weeks. At the conclusion of the study, the incudes of the calves were examined histopathologically. Histopathologically, no necrosis was observed on any ossicle, including the FMT attachment site. Histology did not show evidence of osteoclastic activity or bone resorption at the FMT attachment site. The study concluded there were no permanent changes in ABR thresholds. The evidence

from the animal study results is consistent with a claim of safety as there were no permanent changes in ABR threshold and no notable histopathology.

C. Electrical Testing

A series of tests were conducted on the Vibrant Soundbridge to verify design criteria and device performance with respect to electrical properties and the specifications supporting the safety and effectiveness profile of the device. Where applicable, test protocols were drafted referring to recognized, consensus standards. Other test protocols, as necessary, were drafted by the sponsor to verify design criteria and device performance unique to the Vibrant Soundbridge.

1. Vibrating Ossicular Prosthesis (VORP Model 502)

Where appropriate, the VORP was tested in finished form and passed the following tests: Performance Characterization Test, Implant Protection Verification Test, Electromagnetic Immunity Test, Electromagnetic Emissions Test, and Wireless Device Compatibility Tests.

The Implant Protection Verification Test was performed by providing known input current levels to the demodulation electronics circuitry and measuring the resultant output current. Testing involved providing both direct-coupled and coil-coupled drive currents to the demodulation package as well as testing the device to failure. Test results demonstrated that the demodulation electronics package appropriately passes drive current to the Floating Mass Transducer (FMT) load linearly up to 120 dB SPL equivalent input with less than 5 dB signal loss. Above 120 dB SPL equivalent input, the circuit limits the output current drive to less than 125 dB SPL equivalent during normal coil-coupled operation. Testing using direct-coupled current showed that when tested to failure, the demodulation electronics failed in a safe mode by not conducting any drive currents to the FMT load.

2. Audio Processor (Model 302 and Model 304)

Where appropriate, the Audio Processors were tested in finished form and passed the following tests: Performance Characterization Test, Dielectric Strength and Leakage Current Tests, Electromagnetic Immunity Test, Electromagnetic Emissions Test, and Wireless Device Compatibility Tests.

3. Programmer (Model 600 and Model 700)

Where appropriate, the Programmers were tested in finished form and passed the following tests: Performance Verification Test, Dielectric Strength and Leakage Current Tests, Electromagnetic Immunity Mechanical Testing.

D. Mechanical Testing

A series of tests were conducted on the Vibrant Soundbridge to verify design criteria and device performance with respect to mechanical properties and the specifications supporting the safety and effectiveness profile of the device. Where applicable, test protocols were drafted referring to recognized, consensus standards. Other test protocols, as necessary, were drafted by the sponsor to verify design criteria and device performance unique to the Vibrant Soundbridge.

1. Vibrating Ossicular Prosthesis ( VORP Model 502)

Where appropriate, the VORP was tested in finished form and passed the following tests: Floating Mass Transducer Attachment Release Test, Floating Mass Transducer Temperature Rise Test, Tensile Strength Test, Conductor Link Flex Test, Flex Test, Particulate Matter Tests, Vibration and Shock Tests, Atmospheric Pressure Change Test, and Simulated Distribution Test.

2. Audio Processor (Model 302 and Model 304)

Where appropriate, the Audio Processors were tested in finished form and passed the following tests: Operating Temperature Tests, Attachment Strength Test, Battery Door Strength Test, Vibration Test, Unpackaged Drop Test, and Simulated Distribution Test.

3. Programmer (Model 600 and Model 700)

Where appropriate, the Programmers were tested in finished form and passed the following tests: Operating Temperature Test, Unpackaged Drop Test, and Simulated Distribution Test.

E. Shelf Life Testing

A series of *in vitro* studies were conducted on the Floating Mass Transducer and the Vibrating Ossicular Prosthesis under accelerated conditions of temperature and applied drive current to model the reliability of the device. In addition, real time shelf life studies were conducted on finished, sterile VORPs in their final packaging configuration.

1. Accelerated Life Testing

Accelerated life testing was conducted on the Floating Mass Transducer at an accelerated temperature of 87° C and an accelerated applied drive current of 10 mA. Accelerated life testing was conducted on the Vibrating Ossicular Prosthesis at an accelerated temperature of 87° C. The accelerated life testing results for the Floating Mass Transducer and the VORP implant support a minimum reliability estimate of 97% (95% confidence interval) at ten (10) years.

2. Shelf Life Testing

Shelf life testing was conducted on finished, sterile Vibrating Ossicular Prostheses in their final packaging configuration. Real time shelf life testing is established at two (2) years. The VORP implant is provided sterile, thus expiration dating is established based upon the VORP implant in its final packaging configuration. The VORP did not degrade during the shelf life test period.

The Audio Processors are not provided sterile and are not subject to aging. Thus, no accelerated life testing or shelf life testing was conducted on the Audio Processors.

F. Software Verification/Validation and Statement Regarding Year 2000 Compliance

The Programmers contain software defining the interface for an audiologist's use in modifying the signal output of an Audio Processor.

Software requirements are defined by the sponsor and then developed by an approved subcontractor per 21 C.F.R. § 820.50 (Purchasing controls). Software is controlled by part number and revision level in accordance with the sponsor's Quality System and 21 C.F.R. § 820.40 (Document controls). Software development, verification, and validation activities are documented pursuant to 21 C.F.R. § 820.30 (Design controls), as appropriate.

The software used to program the Vibrant Soundbridge system was developed in conformance to FDA's draft *Guidance for Off-the-Shelf Software Use in Medical Devices* and draft *General Principles of Software Validation*, version 1.1, and is categorized as presenting a minimal hazard to the patient.

Testing and analyses performed verified that the Vibrant Soundbridge is deemed by the sponsor to be Year 2000 (Y2K) compliant. Compliance is based upon the fact that the only devices in the Vibrant Soundbridge System that could potentially be affected by the Y2K phenomenon are software embedded in the Model 600 Programmer and the Model 700 Programmer. The Programmers are not affected by Y2K since their operation is not influenced by, and do not depend upon, knowledge of the date and time.

G. Conclusions of Preclinical Studies

The results of the preclinical studies provided reasonable assurance that the Vibrant Soundbridge was safe for clinical studies and implantation in humans for its intended use.

## IX. Summary of Studies

A. Study Objectives

The study objectives were to determine whether the Vibrant Soundbridge provided a level of useful sound perception (functional gain) and improved subject's satisfaction (self-assessment questionnaires) without having a clinically significant affect upon the patient's residual hearing (air-conduction thresholds).

B. Study Design

The clinical study was designed as a single-subject, repeated measures investigation in which each subject served as her or his own control. The study methods applied a variety of standard, well-known and accepted audiologic diagnostic techniques.

Subjects were evaluated presurgery in an unaided and aided (acoustic hearing aids) condition at the implant ear. Post surgery, subjects were seen for evaluation three times at predetermined intervals (with the Vibrant P Soundbridge) with the last test interval reported at 3-months post activation (5-months post-surgery).

Subjects fit with the Vibrant D Audio Processor had completed all evaluation intervals with the Vibrant P Soundbridge. The patients were then fit and trialled with the Vibrant D Audio Processor for six weeks prior to evaluation for safety and effectiveness of the device.

C. Study Population

A total of fifty-four (54) subjects (pivotal study) with bilateral, moderate to severe sensorineural hearing loss were implanted with the Vibrant Soundbridge (one subject's device did not activate, thus there were 53 subjects evaluated) at ten (10) implanting sites, as illustrated below.

| Site ID | Site Location | Number of Subjects |
|---|---|---|
| US01 | Otologic Center, Kansas City, MO | 10 |
| US02 | House Ear Institute, Los Angeles, CA | 9 |
| US03 | University of Miami, Miami, FL | 7 |
| US04 | Denver Ear Institute, Denver, CO | 5 |
| US07 | Hearing Institute for Children and Adults, San Jose, CA | 6 |
| US08 | Virginia Mason Medical Center, Seattle, WA | 5 |
| US10 | Lenox Hill Hospital, New York City, NY | 2 |
| US11 | University of Michigan, Ann Arbor, MI | 1 |
| US12 | Baptist Medical Center, Oklahoma City, OK | 6 |
| US13 | Indiana University, Indianapolis, IN | 3 |

The age range of the pivotal study subjects was 28 to 86 years, as shown below.

| Age (years) | Number of Subjects | Percentage of Subjects |
|---|---|---|
| 28 – 44 | 11 | 20.4% |
| 45 – 64 | 23 | 42.6% |
| 65+ | 20 | 37.0% |

The distribution of females and males enrolled in the study was substantially equal. Twenty-eight (28) of the subjects were female and twenty-six (26) were male.

Of the pivotal study subjects, forty-four (44/54 or 81.5%) subjects were reported to have an unknown etiology for their hearing loss. Five (5/54 or 9%) subjects had hearing loss attributed to heredity. Two (2/54 or 3.7%) subjects had hearing loss attributed to noise exposure. One (1/54 or 1.8%) subject had hearing loss attributed to presbycusis. One (1/54 or 1.8%) subject had hearing loss attributed to barotrauma. One (1/54 or 1.8%) subject had hearing loss attributed to trauma.

Fifty-one (51/54 or 94.4%) pivotal study subjects indicated the duration of their hearing loss. Duration of hearing loss ranged from less than 1 year to 58 years. The mean duration of loss was 21 years. All subjects were current users of acoustic hearing aids and included in the study only after their amplification devices were found to provide the subject with gain across test frequencies consistent with a well accepted prescriptive formula (NAL-R).

Per the clinical protocol, if there was a difference in the audiologic assessment of a subject's ears, then the patient's "worst" ear was selected for implantation. Twenty-nine (29/54 or 54%) right ears were implanted, and twenty-five (25/54 or 46%) left ears were implanted.

D. Study Period

Investigational study of the Vibrant Soundbridge was authorized in February 1996 (G960015). The investigation was divided into phases with Phase I (pilot study) including five (5) patients implanted at two investigational sites. Enrollment in the pivotal multi-center study included fifty-four (54) patients implanted at ten (10) centers throughout the United States. The Phase IIIa (supplemental safety cohort) study including thirty (30) U.S. subjects implanted at eight (8) centers throughout the United States

The first subject in the pilot study was implanted on October 4, 1996. The first subject in the pivotal study was implanted on March 10, 1998. The last pivotal study subject for the evaluation of the Model 502 VORP with the Model 302 Audio Processor (Vibrant P Soundbridge) completed the 3 months post activation evaluation on August 16, 1999. The first pivotal study subject for the evaluation of the Model 502 VORP with the Model 304 Audio Processor (Vibrant D Soundbridge) was fit on March 30, 1999. The last pivotal study subject for the Vibrant D Soundbridge completed the 6-week evaluation test interval on December 2, 1999. The first U.S. supplemental safety cohort subject was implanted on September 1, 1999. Twenty-nine (29) of the thirty (30) U.S. supplemental safety cohort subjects completed the evaluation period as of the date of the panel meeting, July 20, 2000.

E. Inclusion/Exclusion Criteria

1. Inclusion Criteria

a. Pure-tone audiologic tests suggest a sensorineural hearing loss. Hearing loss in the ear implanted must be equal to or worse than the unimplanted ear.

- Pure-tone air-conduction threshold levels shall fall at or within the levels listed in the following chart.

| Frequency (kHz) | 0.5 | 1 | 1.5 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|
| Lower Limit | 10 | 10 | 20 | 30 | 40 | 40 |
| Upper Limit | 65 | 75 | 80 | 80 | 85 | 85 |

- Pure-tone threshold average as measured at 500Hz, 1000Hz, and 2000Hz in the ear to be implanted must be greater than 30dB.
- Pure-tone air-conduction thresholds for both ears are within 20dB of each other at the above frequencies.
- Air-bone gap at 0.5, 1, 2, and 4 kHz shall be no greater than 10 dB at two or more of these frequencies.
- The subject's word recognition score, using a phonetically balanced word list (NU-6) at 40 dB SL or MCL, is at least 50%.

b. Persons with normal middle ear anatomy and function based on tympanometry and acoustic reflex results who have not previously undergone middle ear surgery and have no history of post adolescent, chronic middle ear infections or inner ear disorders, such as vertigo or Meniere's syndrome.

c. Absence of evidence that hearing loss is of retrocochlear origin.

d. Persons who are currently users of acoustic hearing aids and have used these aids for at least four hours (average) per day for a t least three months prior to evaluation. The subject's hearing aid, in the ear to be implanted, shall be capable of achieving a NAL-R prescription at 500, 1000, 2000 and 3000 Hz. Capable means that the aided threshold at each frequency of the NAL-R prescription is within ± 15 dB.

e. Persons who, after being informed that a different acoustic hearing aid than the one they currently have may provide improved hearing, still request an implant.
f. Persons of age eighteen or older
g. Persons with normal speech and language skills
h. Persons who use English as their primary language.
i. Persons who are psychologically and emotionally stable with realistic expectations.

All enrolled subjects were current users of acoustic hearing aids and met the above-listed selection criteria.

Per the clinical protocol, if there was a difference in the audiologic assessment of a subject's ears, then the subject's worse ear was selected for implantation. Twenty-nine (29/54 of 54%) right ears were implanted and twenty-five (25/54 or 46%) left ears were implanted.

2. Exclusion Criteria

a. Persons with conductive, retrocochlear or central auditory disorders. No persons with absent acoustic reflexes at all frequencies shall be included in the study.
b. Persons whose hearing loss has demonstrated an improving and decreasing fluctuation over a two year period of 15 dB in either direction.
c. Persons suffering from any physical, psychological, or emotional disorder that would interfere with surgery or the ability to perform on test and rehabilitation procedures.
d. Persons who are mentally retarded developmentally delayed or suffering from organic brain dysfunction.
e. Persons not physically or geographically capable of returning for scheduled follow-ups.
f. Persons with skin or scalp conditions that may preclude attachment of the Audio Processor with a magnet.

F. Findings

1. Safety

The safety of the Vibrant Soundbridge was evaluated primarily in terms of the incidence and severity of anticipated adverse events, potential adverse events, and device failures and replacements. Adverse events are based upon information on 81 U.S. subjects (5 subjects from the feasibility study, 54 subjects from the pivotal study, and 22 subjects from the supplemental safety cohort) reported as of May 15, 2000. Adverse event information reported from foreign data was consistent with that reported on the U.S. data. Further assessment of safety was based on the incidence of decreases in residual hearing greater than 10 dB Pure-Tone Average (PTA) measured at 500, 1000, and 2000 Hz.

| | U.S. Patients (n = 81) | |
|---|---|---|
| **Description** | **Reported** | **Unresolved** |
| Device failure[1] | 6 | 0 |
| Transient facial paresis[2] | 2 | 0 |
| Infection[3] | 1 | 0 |
| Episodic dizziness[4] | 2 | 0 |
| Change in residual hearing[5] | 2 | 2 |
| Fullness sensation[6] | 18 | 13 |
| Perforated tympanic membrane[7] | 1 | 0 |
| Altered taste sensation[8] | 7 | 2 |
| Skin irritation[9] | 2 | 0 |
| Transient pain[10] | 13 | 4 |
| Disconnection of FMT[11] | 1 | 0 |

1. Failed devices were removed and patients successfully reimplanted. All failures occurred with a version of the device that is no longer manufactured.
2. In both cases, the investigators reported the facial paresis as unrelated to the surgical procedure or device implantation. Both cases resolved with medical management.
3. Stitch abscess at the inferior aspect of the incision resolved by removing the stitch and prescribed topical and oral antibiotics.
4. Post operative bouts of episodic dizziness resolved without medical intervention.
5. See Clinical Study Results section of the package insert for further information.
6. Perception of this fullness sensation does not affect the individual's ability to use the Vibrant Soundbridge.
7. The tympanic membrane was perforated during the implantation procedure. The perforation was repaired by using fascia.
8. Altered taste sensation can be related to the severing or irritation of the chorda tympani nerve during the implantation procedure. Resolution occurred spontaneously without treatment or surgical intervention.
9. A mild skin irritation over the magnet attachment site was resolved through the use of a weaker strength magnet and/or topical medication.
10. Reports of transient post surgery pain resolved spontaneously without treatment or surgical intervention.

11. Post operatively the device did not activate. During the successful revision surgery, the investigator noted that the FMT had not been in contact with the ossicular chain.

a. Device Failures and Replacements

There were six (6) internal device failures in the clinical investigation. All six (6) subjects completed the three-month post activation prior to device failure. One (1) subject failed to activate two months post surgery. On a worldwide basis, an additional six (6) internal device failures were confirmed. All failures occurred with a version of the device that is no longer manufactured.

The root cause of the device failure was assigned to cyclic fatigue of the bifilar wire in the conductor link of the implanted VORP.. In certain cases, the wire was bent back upon itself into a strained position, thus making it vulnerable to a cyclic failure event. A manufacturing change was instituted by the sponsor to extend and reinforce the transition area between the VORP body and the conductor link. As of July 30, 2000 there have been no failures reported for devices produced with the manufacturing change incorporating the VORP transition sleeve.

After completing the pilot study protocol, one subject was authorized to receive the Model 502 VORP. Data from this subject was included to support the safety, but not the effectiveness, profile for the device in the PMA.

b. Residual Hearing Changes

Fifty-one subjects (51/53 or 96%) had no change (≥10 dB) in the Pure Tone Average (PTA) of 500, 1000, and 2000 Hz. One subject (1/53 or 2%) experienced a change in PTA of 12 dB (decreased) and one subject (1/53 or 2%) experienced a change in PTA of 18 dB (decreased).

The change in average residual hearing for many subjects (39/53 or 74%) measured at 250, 500, 1000, 2000, 4000, 6000, and 8000 Hz was less than or equal to 5 dB, as illustrated in Figure 1. Few subjects (7/53 or 13%) had a decrease in unaided hearing threshold after implantation of greater than 10 dB at 1000, 2000, or 4000 Hz, and few patients (6/53 or 11%) had a decrease in unaided hearing threshold of greater than 15 dB at 250, 500, 6000, or 8000 Hz.

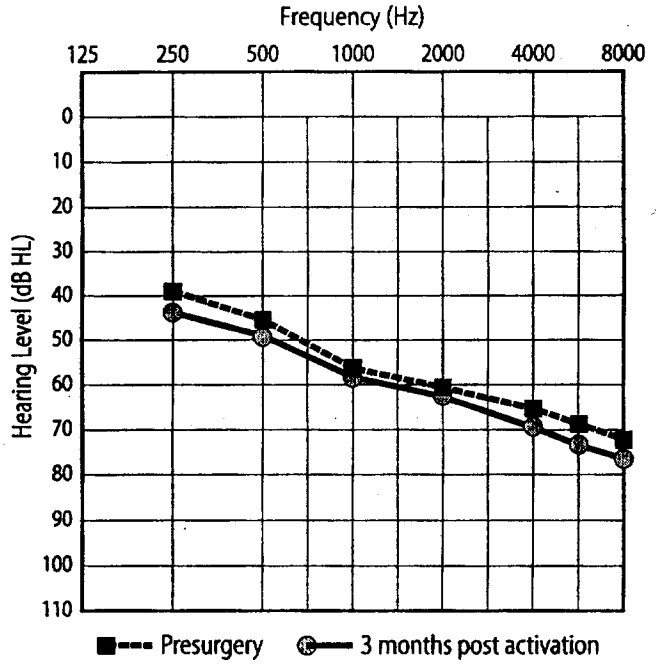


Figure 1. A comparison of mean residual hearing thresholds at presurgery and at 3 months post activation (n=53).

c. Study Discontinuation

During the Vibrant Soundbridge investigational study, no subjects were lost to follow-up.

2. Effectiveness

The effectiveness of the Vibrant Soundbridge was evaluated primarily in terms of whether the device provided a level of useful sound perception (functional gain) and improved perceived benefit and satisfaction compared to the subjects' own hearing aids. The number of subjects supporting each clinical result vary as data are based upon the number of pivotal study patients who completed all test requirements for a particular study endpoint.

a. Sound Clarity and Overall Sound Quality

Subject reports of improved sound clarity and overall sound quality with the Vibrant Soundbridge are based upon three subscales of the Hearing Device Satisfaction Scale (HDSS). Results are illustrated in Figure 2. Forty-two subjects (42/49 or 86%) expressed satisfaction in clearness of sound and tone with the Vibrant P Soundbridge compared to fifteen subjects (15/49 or 31%) whom expressed satisfaction in the clearness of sound and tone of their own hearing aids. Four subjects (4/53 or 8%) were dissatisfied or very dissatisfied with the clearness of sound and tone of the Soundbridge. Forty-four subjects (44/47 or 94%) improved their satisfaction rating of overall sound quality when using their

Vibrant P Soundbridge compared to their own hearing aids. Forty-three subjects (43/49 or 89%) improved their satisfaction rating of sound quality of their own voice when using their Vibrant P Soundbridge compared to their own hearing aids.

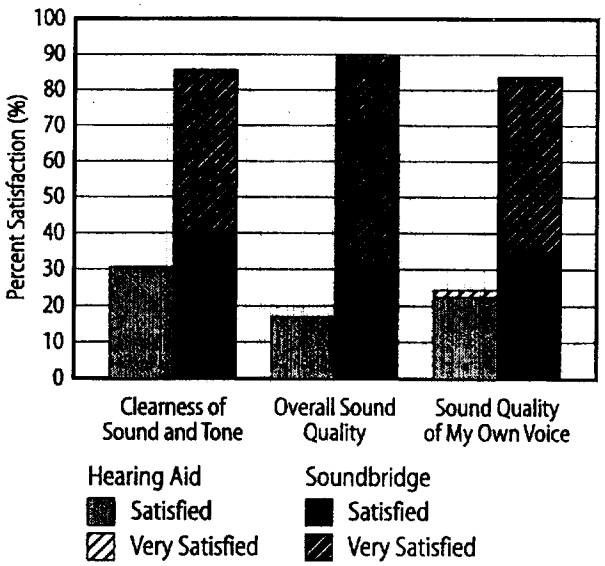


Figure 2. HDSS results: sound clarity and quality measures.

b. Overall Fit and Comfort

Subject reports of better overall fit and comfort with the Vibrant Soundbridge are based upon one subscale of the HDSS. Forty-eight subjects (48/49 or 98%) expressed satisfaction with the overall fit and comfort of the Soundbridge. For the eleven (11) subjects who were dissatisfied with the overall fit and comfort of their own hearing aids, all eleven subjects (11/11 or 100%) were satisfied with the Vibrant Soundbridge.

c. Reduction in Acoustic Feedback

Subject reports of reduction in acoustic feedback with the Vibrant Soundbridge are based upon one subscale of the HDSS. Of the thirty-two (32) subjects who reported acoustic feedback with their own hearing aids, thirty-one subjects (31/32 or 97%) reported no acoustic feedback with their Vibrant Soundbridge.

d. Increased Functional Gain

The Vibrant Soundbridge demonstrated a statistically significant increase in functional gain from 500 Hz through 6000 Hz when compared to a subject's presurgery aided condition.

With the Vibrant P Soundbridge, there was a statistically significant increase in functional gain at 1000 Hz at $p < 0.01$, and for the frequencies of 2000 Hz, 3000 Hz, 4000 Hz, and 6000 Hz at $p < 0.001$, compared to the subjects' own hearing aid, as illustrated in Figure 3.

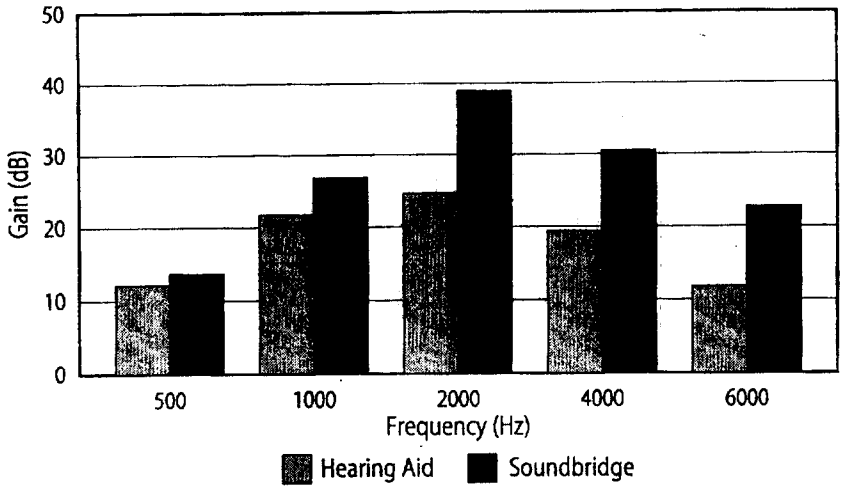


Figure 3. Functional Gain for presurgery hearing aid and 3 months post activation for the Vibrant P Soundbridge (n=53).

At 500 Hz most (43/53 or 81%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 1000 Hz most (44/53 or 83%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 2000 Hz most (52/53 or 98%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 4000 Hz most (48/53 or 91%) patients had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 6000 Hz most (47/53 or 89%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 8000 Hz most (13/13 or 100%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid.

With the Vibrant D Soundbridge, functional gain was significantly increased ($p < 0.001$) for the frequencies of 500 Hz, 1000 Hz, 2000 Hz, 3000 Hz, 4000 Hz, and 6000 Hz, compared to the subjects' own hearing aid, as illustrated in Figure 4.

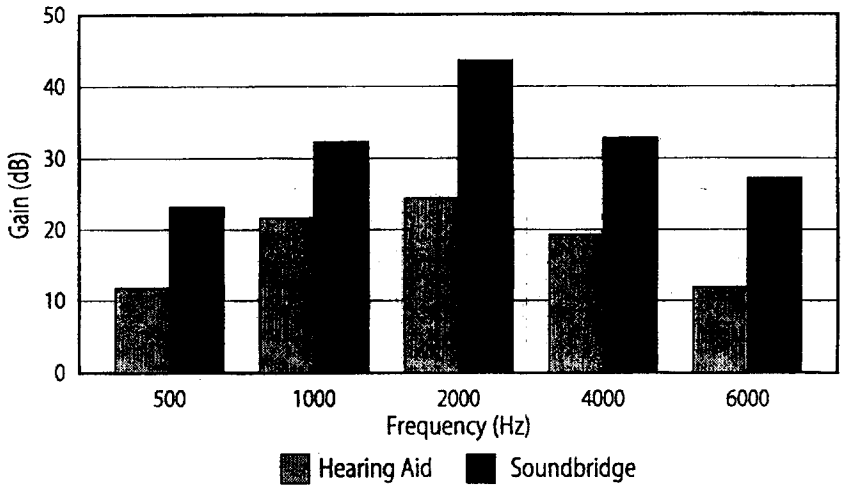


Figure 4. Functional Gain at presurgery hearing aid and 6-week evaluation for the Vibrant D Soundbridge (n=50).

At 500 most (46/50 or 92%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 1000 Hz most (49/50 or 98%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 2000 Hz most (50/50 or 100%) subjects had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 4000 Hz most (47/50 or 94%) patients had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 6000 Hz most (43/50 or 86%) patients had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid. At 8000 Hz most (13/13 or 100%) patients had a functional gain that was equal (within 5 dB) or increased from the functional gain of the subject's own hearing aid.

e. Perceived Benefit in Many Listening Situations

Subject's perceived benefit in many listening situations with the Vibrant Soundbridge is based upon subjective reporting using the Profile of Hearing Aid Performance (PHAP), Cox and Gilmore, 1990. Additionally, subject's improved satisfaction rating of the effectiveness of the Vibrant Soundbridge in background noise compared to their own hearing aids is supported by one subscale of the HDSS.

With the Vibrant P Soundbridge, the subjects as a group reported significant improvement with the Soundbridge compared to their own hearing aids on all seven subscales of the PHAP, as illustrated in Figure 5.

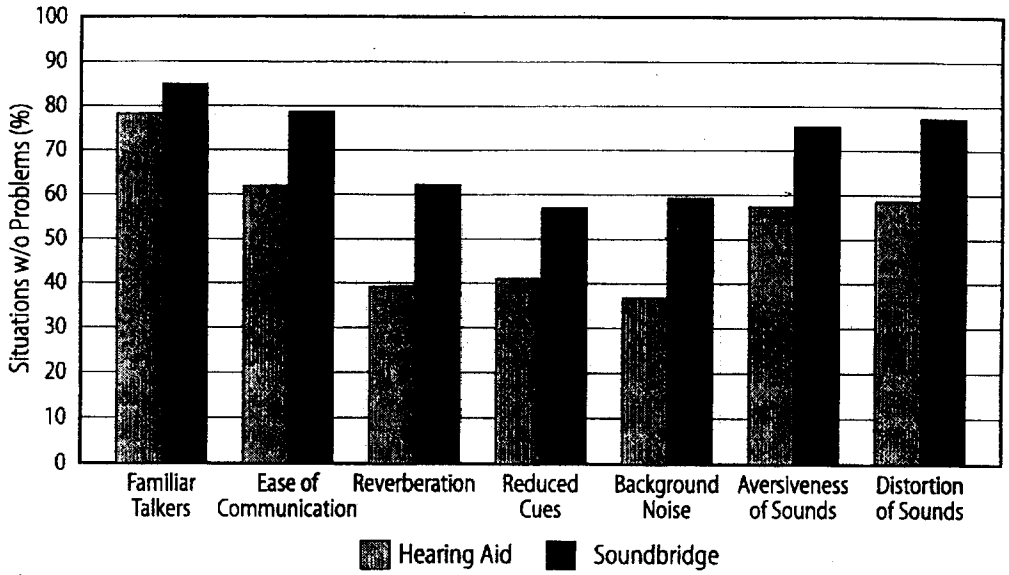


Figure 5. Mean PHAP responses at presurgery and 3 months post activation for the Vibrant P Soundbridge (n=51).

For individual subject analysis on the PHAP with the Vibrant P Soundbridge, significant improvement was based upon comparison to critical difference scores at a 95% confidence interval, as described below:

- Familiar Talkers: 8 out of 51 patients (16%)
- Ease of Communication: 14 out of 51 patients (27%)
- Reverberation: 24 out of 51 patients (47%)
- Reduced Cues: 20 out of 51 patients (39%)
- Background Noise: 27 out of 51 patients (53%)
- Aversiveness of Sounds: 13 out of 51 patients (25%)
- Distortion of Sounds: 15 out of 51 patients (29%)

With the Vibrant D Soundbridge, the subjects as a group reported significant improvement with the Soundbridge compared to their own hearing aids on all seven subscales of the PHAP, as illustrated in Figure 6.

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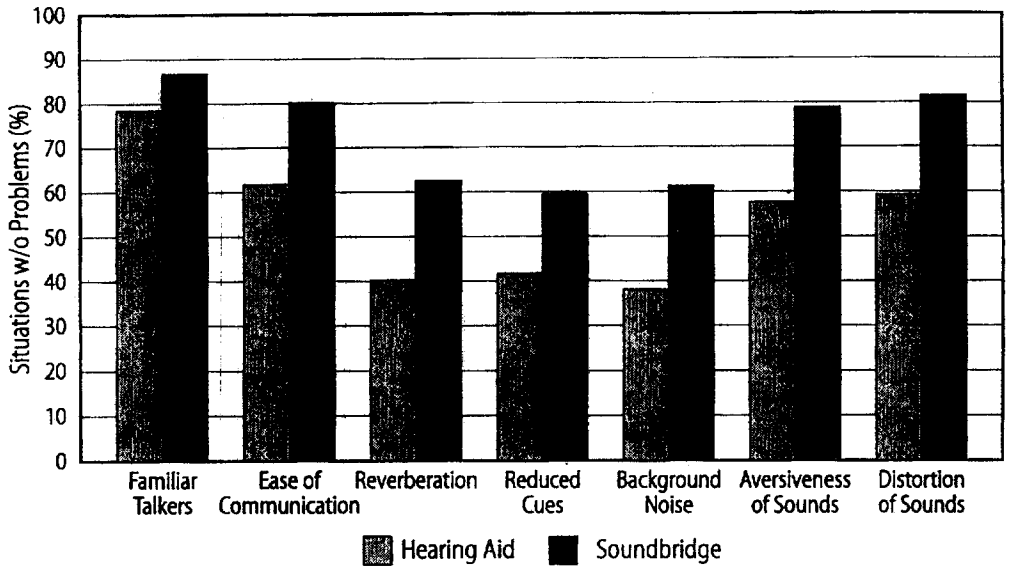


Figure 6. Mean PHAP responses at presurgery and 6-week evaluation of the Vibrant D Soundbridge (n=50).

For individual subject analysis on the PHAP with the Vibrant D Soundbridge, significant improvement was based upon comparison to critical difference scores at a 95% confidence interval, as described below:

- Familiar Talkers: 9 out of 50 patients (18%)
- Ease of Communication: 15 out of 50 patients (30%)
- Reverberation: 24 out of 50 patients (48%)
- Reduced Cues: 18 out of 50 patients (36%)
- Background Noise: 28 out of 50 patients (56%)
- Aversiveness of Sounds: 21 out of 50 patients (42%)
- Distortion of Sounds: 17 out of 50 patients (34%)

The results from the HDSS subscale for background noise is supported by the PHAP results reported above. Forty-three subjects (43/49 or 88%) improved their satisfaction rating of the effectiveness of the Soundbridge in background noise compared to their own hearing aids.

f. Reduced Maintenance Issues

Subjects' satisfaction in reduced maintenance issues with the Vibrant Soundbridge due to cerumen and moisture accumulation is based upon one subscale of the HDSS. Forty-five subjects (45/46 or 98%) expressed satisfaction with cleaning and maintenance issues with the Vibrant P Soundbridge, such as those due to cerumen and moisture accumulation. For the fourteen (14) subjects who were dissatisfied with cleaning and maintenance of their own hearing aids, all fourteen subjects (14/14 or 100%) were satisfied with the Vibrant Soundbridge.

Cerumen cannot accumulate on the Soundbridge since it does not sit in the ear canal.

g. Speech Perception Results

Speech perception results are based upon testing of the Vibrant Soundbridge and the subjects' own hearing aid in a controlled soundfield environment (i.e., NU-6 word scores, SPIN-low predictability word scores) and upon the Soundbridge Hearing Aid Comparison Questionnaire (SHACQ), a non-validated assessment tool developed by Symphonix Devices, Inc. The SHACQ was administered to subjects post operatively on a one-time basis.

Speech perception testing in a controlled environment demonstrated **equivalent group mean** results between the Vibrant Soundbridge and the subjects' own hearing aid. However, as reported on the SHACQ, when listening to speech, the Vibrant Soundbridge was preferred over the subjects' own hearing aids in various listening situations. Thirty-three subjects (33/43 or 86%) preferred the Vibrant Soundbridge compared to their own hearing aids when listening to speech outdoors. While listening to speech in quiet environments, forty-one subjects (41/43 or 95%) preferred the Vibrant Soundbridge compared to their own hearing aids. While listening to speech in a restaurant, thirty-five subjects (35/40 or 88%) preferred the Vibrant Soundbridge compared to their own hearing aids. Thirty-eight subjects (38/44 or 86%) preferred the Vibrant Soundbridge over their own hearing aids when listening to speech on the television. While listening to speech on the radio, thirty-five subjects (35/40 or 88%) preferred the Vibrant Soundbridge to their own hearing aids.

h. Conclusions of Clinical Study

Data from the U.S. clinical trial and reports of foreign data with up to three years of implantation with the Vibrant Soundbridge provides reasonable assurance that the incidence rate of adverse reactions, surgical complications, and device-related problems is low. Clinical issues, if any, generally occur within a short time of surgery, resolve without surgical intervention, or do not pose an undue risk to patient safety.

Benefit with the Vibrant Soundbridge is evident at activation (2 months post surgery) and is not dependent on a protracted training or acclimation period. Available evidence does not reasonably suggest patient performance with the device varies over time.

## X. Conclusion Drawn from the Studies

The results of the preclinical and clinical studies provide reasonable assurance of the safety and effectiveness of the Vibrant P Soundbridge and the Vibrant D Soundbridge for the patient population, sensorineural hearing loss characteristics, and specified indications for use.

Although the potential exists for minor differences in physiological response by gender for the target population, the minimal number of clinically significant findings does not indicate that gender differences are of clinical importance for this device.

## XI. Panel Recommendation

At an advisory meeting held July 20, 2000, the Ear, Nose, and Throat Devices Panel recommended that the Symphonix Devices, Inc. Vibrant P Soundbridge and Vibrant D Soundbridge be approved with conditions. These conditions included changes to the device labeling and an addition to the Post Market Surveillance Study Plan.

**Labeling:** The Panel recommended that labeling be reworded to provide clearer meaning to medical professionals and prospective patients regarding the results of the clinical investigation.

**Post Market Surveillance Study Plan:** The Panel recommended that the sponsor monitor device extrusion as a potential adverse event in the Phase IIIa patient population.

## XII. FDA Decision

FDA issued an approval order on August 31, 2000.

Labeling provided includes two patient brochures. One is intended to provide information to the patient to assist in making the decision whether to have the device implanted and the second is to assist the patient in the use of the device after implantation.

The manufacturing facility was found to be in compliance with device Good Manufacturing Practices (GMP). Final GMP approval was dated August 24, 2000.

## XIII. Approval Specifications

- Directions for use: See attached labeling.
- Warnings, hazards to health from use of the device: See Indications, Contraindications, Warnings and Precautions.
- Post approval requirements and restrictions: See Approval Order.