

## **Ear, Nose, and Throat Devices Panel Questions**

**November 8, 2013**

1. The pivotal study results indicate that 34% (17 of 50) of subjects' residual hearing sensitivity is at the profound/total hearing loss levels at the 6-month interval. Among the subjects who had data available beyond the 6-month interval, 5 developed profound/total hearing loss at a later interval (one at 12 months, two at 18 months, one at 36 months, and one at 48 months). Please discuss the following:
  - a. The clinical significance of this residual low-frequency hearing loss at the 6- and 12-month intervals, and
  - b. Whether the limited long-term residual hearing loss data raise safety concerns for the Hybrid L24 implant system.
2. In the PMA, the applicant states that threshold changes  $\leq 30$  dB are "unlikely to impact functional low-frequency hearing" and changes  $> 30$  dB are "likely to impact functional low-frequency hearing." Please discuss the clinical significance of the residual low-frequency hearing loss between 10 and 30 dB experienced by 30% (15 of 50) of the subjects at 6 months.
3. The pivotal study reveals that 34% (17 of 50) of subjects who received a Hybrid L24 implant exhibited a profound loss (90+ dB HL) or total loss (no measurable hearing) for their residual low-frequency hearing at the 6-month interval following implantation. As part of the analyses of the pivotal study data, the applicant analyzes effectiveness data based on the dichotomization of the subjects' status of residual low-frequency hearing sensitivity – Group 1 has subjects whose hearing loss is in the range of severe or better (moderate, moderately-severe, and severe), while Group 2 has subjects whose hearing loss is in the range of profound (profound and total). Please discuss the appropriateness of the applicant's classification and analysis of hearing loss data which they use to characterize the clinical significance of residual hearing losses observed in the study.
4. In the proposed labeling, the applicant states that the Hybrid L24 electrode may be inserted either via a cochleostomy or the round window. However, all cases in the pivotal clinical study were inserted via cochleostomy. In a European study conducted using the Hybrid L24 implant, 64 of 66 subjects were implanted using the round window approach. Any comparison between the US pivotal and the European study to assess impact of the surgical approach on the safety and effectiveness of the Hybrid L24 implant is limited due to differences in study populations and study design. Please discuss whether the currently available information supports labeling the Hybrid L24 implant for both the cochleostomy and the round window approach.

5. The proposed Indications for Use does not specify any requirement for a trial of appropriately fit hearing aids. However, 3 subject candidates underwent the trial of appropriately fit hearing aids as part of the study requirements decided to pursue hearing aid amplification in lieu of the Hybrid L24. Given the high incidence of profound or total loss of residual low frequency hearing (22/50 subjects, 44%), please comment on the appropriateness of requiring a hearing aid trial with properly fit hearing aids. If you believe such a criterion is necessary, please also comment on the minimum length of such a hearing aid trial prior to implantation.
6. The proposed Indications for Use does not explicitly specify unilateral implantation. All subjects in the pivotal clinical study were implanted unilaterally with the Hybrid L24 device. In the Hybrid test condition, a small portion of study subjects performed poorer for CNC Words (4.0%), CNC Phonemes (10.0%), and the AzBio Sentences in Noise (12.0%), as compared to their pre-operative performance. In the Combined test condition, where the subjects used their contralateral residual low-frequency hearing, all subjects performed equal or better on these assessments. Please discuss whether the Hybrid L24 should be explicitly indicated for only unilateral implantation to reduce the possibility of residual low-frequency hearing loss in the contralateral ear.
7. The clinical cohort primarily consisted of subjects aged 37 years and older (only one subject was age 23 years old). The applicant proposes a minimum of 18 years for the indicated patient population. FDA regulations for medical devices consider the age group of 18 through 21 years as “transitional adolescents” and include this group in the pediatric population (21 years old or younger). Please discuss whether there is sufficient information to extrapolate the use of this device to patients 18 years and older. In your discussion please consider factors such as psychological competence, neurocognitive development, and the presence of congenital syndromes for the transitional adolescent population.
8. If the device is approved, the applicant is proposing two post-approval studies: 1) extended follow-up of the premarket pivotal study subjects for 5 years after device activation to monitor long-term safety and effectiveness, and 2) a new enrollment study to monitor postmarket safety and effectiveness. Please discuss the following:

Extended Follow-up of Premarket Cohort

- a. Please discuss the appropriateness of this study population (existing premarket cohort who agree to participate in an IDE study to evaluate the new investigational features of the CP900 series) to evaluate the long-term safety and effectiveness of the Hybrid L24 Implant System, with specific considerations of the audiological measurements and a potential carry-over effect due to the on/off function of investigational features.

- b. The applicant has proposed that the device effectiveness will be assessed by comparing within-subject differences measured by CNC and AzBio tests between the preoperative and 60 months post-activation interval. Considering the proposed study population, please discuss how device effectiveness should be measured in this study.
- c. The applicant has proposed to continue to follow the subjects for 5 years post-activation of the device. Please discuss the appropriate duration for this study.

*New Enrollment Study*

- d. The applicant plans to assess device effectiveness by comparing within subject differences measured by CNC and AzBio tests between pre-operative and 36 months. Please discuss if there are any additional long term effectiveness endpoints that should be evaluated in the postmarket setting.
- e. The applicant has proposed to collect data on patient reported outcomes by administering a modified device use questionnaire (DUQ) and health utility index (HUI) questionnaire. Please discuss if there are any other additional patient reported outcomes to be evaluated.
- f. The applicant has proposed to follow the subjects for 3 years post-activation of the device. Please discuss the appropriate duration for this study.
- g. Please discuss if there are any additional considerations that need to be taken into account for the new enrollment study.