SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Cochlear Implant System

Device Trade Name: MED-EL Cochlear Implant System

Device Procode: MCM

Applicant's Name and Address: MED-EL Corp.
Elektromedizinsiche Geraete GmbH
Fürstenweg 77a
6020 Innsbruck
Austria

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P000025/S129

Date of FDA Notice of Approval: October 3, 2024

The original PMA (P000025) for the MED-EL Cochlear Implant System was approved on August 20, 2001. The original device was intended to provide the opportunity to detect and recognize auditory information through electrical stimulation of the auditory nerve for bilateral, severe to profoundly hearing-impaired individuals (ages 18 months and older) who obtain little or no benefit from conventional acoustic amplification in the best- aided condition. (SSED to support the indication is available on the CDRH website: http://www.accessdata.fda.gov/cdrh_docs/pdf/P000025b.pdf). The indications for use were also expanded in P000025/S084 and P000025/S104.

The current panel track supplement was submitted to expand indications for the MED-EL Cochlear Implant System in individuals 18 years of age and older with bilateral, moderate to profound sensorineural hearing loss (SNHL) who obtain limited benefit from appropriately-fit hearing aids in the ear(s) to be implanted. In addition, the applicant submitted several marketing claims on hearing preservation (HP) rates for the MED-EL implant FLEX electrode series in this panel track supplement.

II. INDICATIONS FOR USE

The MED-EL Cochlear Implant System is intended to evoke auditory sensations via electrical stimulation of the auditory pathways for individuals with debilitating sensorineural hearing loss who obtain limited benefit from acoustic amplification in the ear(s) to be implanted and is indicated for the following patient populations:

- Individuals of eighteen (18) years of age or older with bilateral moderate to profound sensorineural hearing loss who obtain limited benefit from appropriately fit hearing aids.

These individuals typically demonstrate a low-frequency pure-tone average of greater than 40 dB HL (at 250 Hz, 500 Hz, and 1000 Hz) and thresholds not better than 65 dB HL at 3000-8000 Hz. Limited benefit from hearing aids is defined by test scores of 50% correct or less in the ear to be implanted and 60% or less in the non-implant ear on recorded tests of monosyllabic word recognition (Consonant-Nucleus-Consonant [CNC] Words).

- MED-EL strongly recommends a hearing aid trial prior to implantation (if not already completed), but radiological evidence of cochlear ossification may preclude a hearing aid trial.

III. CONTRAINDICATIONS

An individual must not be implanted:

- if the individual is known to be intolerant of the materials used in the implant (including medical grade silicone, platinum, iridium, titanium and parylene c);
- if there is an absence of cochlear development;
- if the cause of deafness is non-functionality of the auditory nerve and/or the upper auditory pathway;
- if external or middle ear infections are present or if the tympanic membrane is perforated in the ear to be implanted;
- if there are medical contraindications to surgery of the middle and inner ear and anesthesia as required;
- if an anatomic situation is present that would prevent appropriate placement of the stimulator housing and recessing the pins in the bone of the skull or prevent placement of the chosen electrode array into the cochlea, using the implant shall be carefully considered prior to surgery;
- if the psychological status of the individual is unstable or
- if the individual has unrealistic expectations.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MED-EL Cochlear Implant System product labeling.

V. DEVICE DESCRIPTION

MED-EL Cochlear Implant System

No design changes to the approved devices in the MED-EL Cochlear Implant System are required for the new indications.

The MED-EL Cochlear Implant System consists of the following main components:

- Cochlear Implants (consisting of a stimulator, a coil with a magnet within its center, a variant of an active electrode, a reference electrode and an electrically evoked compound action potential reference electrode):

Mi1250 SYNCHRONY 2 (PIN),
Mi1260 SONATA 2,
Mi1210 SYNCHRONY ST,
Mi1200 SYNCHRONY (PIN),
Mi1050 CONCERTO 2 (PIN),
Mi1000 MED-EL CONCERT (PIN),
SONATATI100

- Processors (single unit processor or Behind-The-Ear (BTE); For BTE processors, an external coil containing a magnet of various strengths for positioning and holding it at the site above the implant by attracting to the magnet inside the implant and a driver for the RF inductive stage):
  SONNET 2 (EAS),
  SONNET (EAS),
  RONDO 3,
  RONDO 2,
  RONDO

- Fitting / Apps:
  MAX Programming Interface
  HearCare MED-EL
  MAESTRO 10 and above
  AudioKey 2 and above

In the MED-EL Cochlear Implant System, the audio processor analyzes the sound signal from the microphone according to the speech coding strategy programmed into the audio processor and transforms it into a coded electrical signal that is sent to the externally worn coil. This coded signal contains information about how the individual electrodes of the implant should be stimulated so sound can be perceived. The coil is magnetically held in place over the implant and sends the coded signal across intact skin to the MED-EL cochlear implant via an inductive link. The energy necessary for stimulation is also sent via the inductive link. The electronics within the MED-EL cochlear implant decode the signals received by the internal secondary coil and sends a corresponding pattern of stimulation pulses to the individual electrodes of the active electrode array. These stimulation pulses excite action potentials which travel along the auditory nerve to the brain, where the brain can categorize the sound and assign meaning. Within the MED-EL Cochlear Implant System, the MAESTRO software together with the MAX Programming Interface and HearCare MED-EL app serves to allow programming of the system components to provide access to speech for the user.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The most common alternative treatment of moderate to profound bilateral high-frequency sensorineural hearing loss is the use of conventional air conduction hearing aids. Conventional air conduction hearing aids are often effective for this population unless speech discrimination becomes significantly compromised. Patients may also choose to forego obtaining a hearing device and pursue rehabilitation via speech reading and/or sign language training. Each of these alternatives has its own advantages and disadvantages. A patient should fully discuss the

alternatives with his/her physician and audiologist in order to select the treatment that best meets his/her expectations and lifestyle.

VII. MARKETING HISTORY

In all markets apart from the US, the indications for use for the MED-EL Cochlear Implant System are defined more broadly for individuals (both adults and children). This supplement now better aligns the indication criteria for individuals eighteen (18) years of age or older in the US with the approvals currently held in over 134 countries globally:

Albania, Algeria, Argentina, Armenia, Aruba, Australia, Austria, Azerbaijan, Bahamas, Bahrain, Bangladesh, Belarus, Belgium, Benin, Bhutan, Bolivia, Bosnia and Herzegovina, Brazil, Bulgaria, Cameroon, Canada, Cayman Islands, Chile, China, Colombia, Costa Rica, Côte d'Ivoire, Croatia, Cuba, Cyprus, Czechia, Denmark, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Ethiopia, Finland, France, Gabon, Georgia, Germany, Ghana, Greece, Guatemala, Honduras, Hong Kong, Hungary, Iceland, India, Indonesia, Iran, Iraq, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kazakhstan, Kenya, Korea (the Republic of), Kosovo, Kuwait, Kyrgyzstan, Latvia, Lebanon, Libya, Lithuania, Luxembourg, Macao, Macedonia, Malawi, Malaysia, Mali, Malta, Mexico, Moldova, Mongolia, Montenegro, Morocco, Myanmar, Namibia, Nepal, Netherlands, New Zealand, Nigeria, Norway, Oman, Pakistan, Palestine, Panama, Paraguay, Peru, Philippines, Poland, Portugal, Qatar, Romania, Russian Federation, Saudi Arabia, Senegal, Serbia, Singapore, Slovakia, Slovenia, South Africa, South Sudan, Spain, Sri Lanka, Sudan, Sweden, Switzerland, Syrian Arab Republic, Taiwan, Tajikistan, Tanzania, Thailand, Togo, Trinidad and Tobago, Tunisia, Turkey, Uganda, Ukraine, United Arab Emirates, United Kingdom, United States, Uruguay, Uzbekistan, Venezuela, Viet Nam, Yemen, Zimbabwe

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the implantation and use of the MED-EL Cochlear Implant System:

- Partial or total loss of residual hearing, either suddenly or over time
- Vertigo, dizziness, or balance problems that did not exist preoperatively or worsened postoperatively
- Facial nerve problems including injury and unintended stimulation
- Meningitis
- Perilymphatic fistulae
- Tinnitus that did not exist preoperatively or worsened postoperatively
- Implant migration/extrusion
- Skin flap problems
- Device-related problems including programming problems and device failure requiring explantation/reimplantation.

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

The pre-clinical studies that were previously submitted to FDA in the original PMA (P000025) and its supplements continue to support the safety and effectiveness of the commercially available MED-EL Cochlear Implant System. No additional preclinical studies were required to evaluate the safety of MED-EL Cochlear Implant System for the treatment of expanded adult indications or the performance statements on hearing preservation. The previously approved supplements which support the device, and its components are listed below.

Table 1: Summary of System/Device Components and Approvals

Device	Approval Reference
Cochlear Implants:	
Mi1250 SYNCHRONY 2 (PIN) Mi1260 SONATA 2 Mi1210 SYNCHRONY ST Mi1200 SYNCHRONY (PIN) Mi1050 CONCERTO 2 (PIN) Mi1000 MED-EL CONCERT (PIN) SONATATI[100]	P000025/S110 P000025/S114 P000025/S103 P000025/S079 P000025/S123 P000025/S050 & S058 P000025/S021
Processors:	
OPUS 1 OPUS 2 RONDO RONDO 2 RONDO 3 SONNET SONNET 2	P000025/S023 P000025/S029 P000025/S062 P000025/S099 P000025/S116 P000025/S078 P000025/S112
Fitting:	
MAX Programming Interface MAESTRO 10 and above HearCare MED-EL AudioKey 2 and above	P000025/S077 P000025/S131 P000025/S126 P000025/S117

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a pivotal clinical study to establish a reasonable assurance of safety and effectiveness of cochlear implantation with the MED-EL Cochlear Implant System for moderate to profound hearing loss in the US under IDE # G170111. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented in "1. G170111 IDE STUDY – Expanded Indications for Use" below. In addition, the applicant proposed hearing preservation claims/performance statements that are supported with real-world data (RWD) from the applicant's registry database (Claims #1 through #5), as well findings from temporal bone studies (Claim #6). A summary of the real-world evidence (RWE) is presented in "2. Residual Hearing Preservation" below.

1. **G170111 IDE STUDY – Expanded Indications for Use:**

As stated above, the applicant conducted a pivotal clinical study to establish a reasonable assurance of safety and effectiveness of the MED-EL Cochlear Implant System for individuals 18 years of age and older with bilateral, moderate to profound SNHL in the US and Canada under IDE #G170111. The clinical study and results are described below.

A. Study Design

Participants were enrolled between April 26, 2018, and March 27, 2023. The database for this Panel Track Supplement reflected data collected through March 27, 2023, and included 44 participants. This multicenter, prospective IDE clinical study used an open-label, single-arm, repeated-measures design, where each participant served as their own control. The database for this panel track supplement reflected data collected through March 27, 2023, and included 44 participants. There were five investigational sites (four academic medical centers in the United States (US) and one academic medical center in Canada).

Two co-primary endpoints were tested using inferential statistics to reject the null hypothesis. Continuous variables were summarized using mean, median, inter-quartile range, minimum, and maximum values. Categorical variables were summarized using counts and percents. The co-primary endpoints were tested at the one-sided alpha = 0.025 level of significance. A sample size of 50 would yield approximately 90% power assuming the true change in mean Consonant-Nucleus-Consonant (CNC) word score is 24.4 with a standard deviation of 21.9 and the true change in mean AzBio sentence score is 15 with a standard deviation of 8.4. However, though the calculated sample size was 50 subjects providing a statistical power of 90%, the final sample size was 44 and the effectiveness analyses included 43 subjects for the intent-to-treat (ITT) population and 42 subjects for the per-protocol (PP) population. One subject with no post-activation data was completely excluded from the primary analyses and the missing data of another subject was imputed using last observation carried forward method. Due to the reduction in the actual sample size from the planned number of participants, the statistical power of the study might have been reduced.

a. *Clinical Inclusion and Exclusion Criteria*

Enrollment in G170111 was limited to participants who met the following inclusion criteria:

- Individuals 18 years of age or older at the time of implantation
- Bilateral moderate to profound SNHL
    - Low-frequency pure-tone average (LFPTA at 250, 500, and 1000 Hz) greater than 40 dB HL
    - High-frequency thresholds not better than 65 dB HL (3000 Hz – 8000 Hz)
- CNC word score in quiet of 10%-60% in the ear to be implanted and 70% or less in the non-implanted ear
- Sensorineural hearing loss, demonstrated by an air-bone gap of less than or equal to 10 dB HL
- Evidence of appropriately fit hearing aids as determined by the audiologist

- Bilateral hearing aids should be considered standard of care, except in situations where the audiologist, physician, or potential subject determines that unilateral fit is optimal
- Hearing aid fit should be verified through accepted measures such as functional gain or real-ear verification
- If appropriately fit hearing aids have not been worn within the last year, a 30-day hearing aid trial must be completed prior to enrollment in the study
- Fluent in English
- No radiographic contraindications
- Ability to undergo general anesthesia
- Appropriate motivation and expectation levels
- Stated willingness to comply with all study procedures for the duration of the study

Participants were not enrolled in the study if they met any of the following exclusion criteria:

- Evidence that hearing loss was retrocochlear in origin
- Active middle ear infection
- Skin or scalp condition precluding use of external audio processor
- Suspected cognitive impairment or organic brain dysfunction
- History of prior use of a hearing implant

b. *Follow-up Schedule*

Eligible participants received a MED-EL Cochlear Implant System (SYNCHRONY or SYNCHRONY 2) within 4 months of completing baseline testing. Each participant was fit about 2-6 weeks after surgery with a compatible external audio processor (SONNET EAS/SONNET 2 EAS and/or RONDO/RONDO 2/RONDO 3 Audio Processor). All participants were scheduled to return for follow-up examinations at 1, 3, 6, and 12 months after fitting of the audio processor. Audiometric thresholds, word recognition scores in quiet, and sentence recognition scores in noise were measured at each study visit after surgery and compared to results before surgery. Information on adverse events was collected and reported as the number and proportion of participants experiencing an adverse device effect (ADE). Data collected at 6 months after fitting was used to analyze the primary safety and effectiveness endpoints. Table 1 below shows key timepoints and outcome measures.

Table 1: Schedule of Events Table

		Candidacy/ Pre-op	Surgery	Activation	1 month post-activation	3 months post-activation	6 months post-activation	12 months post-activation
	Informed Consent	X						
	Medical Assessment	X						
	Surgery		X					
	Tympanometry	X						
	Unaided thresholds	X		X	X	X	X	X
Implant Ear	CNC Words 60 dB SPL (Aided)	X			X	X	X	X
Non-implant Ear		X						
Implant Ear	AzBio 60 dB SPL +10 dB SNR (Aided)	X			X	X	X	X
Everyday Condition	AzBio 60 dB SPL +10 dB SNR (Aided)	X			X	X	X	X
Everyday Condition	*OPTIONAL: AzBio 60 dB SPL +5 dB SNR (Aided)*	*X*			*X*	*X*	*X*	X
	APHAB	X			X	X	X	X
	SSQ	X			X	X	X	X

c. *Clinical Endpoints*

Table 2 below lists the study objectives and endpoints. Both co-primary endpoints had to achieve significance and reject their null hypothesis for the study to be considered successful.

Table 2: IDE Study G170111 Objectives and Endpoints

Objectives	**Endpoints**
Primary	
To demonstrate the effectiveness of MED-EL cochlear implants in adults with bilateral moderate to profound	1. Mean improvement of 10 percentage points or more on Consonant-Nucleus-Consonant (CNC) Words with the cochlear implant at 6 months after activation compared to pre-operative aided CNC word score in the implant ear.
	2. Mean improvement of 10 percentage points or more on AzBio Sentences in noise with the cochlear implant at 6 months after activation compared to pre-operative aided AzBio sentence score in the implant ear.

Objectives	Endpoints
sensorineural hearing loss	
Secondary	
To demonstrate the effectiveness and safety of MED-EL cochlear implants in adults with bilateral moderate to profound sensorineural hearing loss	1. Number and percentage of subjects with similar or better AzBio sentence scores in noise at 6 months after activation compared to baseline in the everyday listening condition. Similar is defined as within 10 percentage points. Better is an improvement of 10 percentage points or more. The everyday listening condition is the subject's daily wearing configuration.
	2. Similar or better responses on the Abbreviated Profile of Hearing Aid Benefit (APHAB) and Speech, Spatial and Qualities of Hearing Scale (SSQ) questionnaires in the everyday listening condition at 6 months after activation compared to baseline.
	3. Preservation of unaided hearing thresholds in the implant ear at 6 months after activation compared to baseline, defined as complete (> 75%), partial (25-75%), minimal (< 25%), or none (no detectable hearing).
	4. Number and proportion of subjects experiencing an adverse device effect (ADE) for the duration of the study.

B. Accountability of Study Cohort

A total of 84 people were consented for baseline testing. Forty of those 84 potential subjects did not meet entry criteria (screen failures) or decided not to participate in the study (attrition). The remaining 44 participants completed enrollment and received the implant, resulting in 44 out of a goal of 50 subjects (88%) enrolled in the study. Forty-two of 44 participants (95.5%) completed the primary endpoint at six months after activation, and 40 of 44 participants (90.9%) completed participation in the study through 12 months after activation.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are provided in Table 3 below. The mean age at implantation was 68.1 years. Nineteen of 44 participants (43.2%) were female, and 25 of 44 participants (56.8%) were male. Nineteen of 44 participants (43.2%) were implanted in the left ear, and 25 of 44 participants (56.8%) were implanted in the right ear. The mean CNC word score in quiet at baseline was 26.5%, while the mean AzBio sentence score in noise was 23.5% in the ear to be implanted at baseline. Nineteen participants received the FLEXSOFT electrode array, and 25 participants received the FLEX28 electrode array.

Table 3: Demographic and Baseline Characteristics

Characteristic	Subjects
Sex	
Female	43.2% (19/44)
Male	56.8% (25/44)
Age (years)	68.1 ± 15.4 (44) 71.1 (16.1) [23.0,91.5]
Race	
American Indian	No records.

Characteristic	Subjects
Asian	No records.
Black or African American	4.5% (2/44)
Native Hawaiian or Other Pacific Islander	No records.
White	70.5% (31/44)
Other	4.5% (2/44)
Ethnicity	
Not recorded	20.5% (9/44)
Not Hispanic or Latino	77.3% (34/44)
Hispanic or Latino	2.3% (1/44)
Ear to be implanted	
Left	43.2% (19/44)
Right	56.8% (25/44)
Implanted ear CNC percent correct (%)	26.5 ± 12.4 (44) 27.0 (19.0) [10.0,48.0]
Non-implant ear CNC percent correct (%)	38.0 ± 17.8 (44) 37.0 (27.0) [0.0,70.0]
AzBio Sentences in Noise (+10 dB SNR): implanted ear (% correct)	23.5 ± 17.3 (44) 19.5 (27.0) [0.0,67.0]
AzBio Sentences in Noise (+10 dB SNR): both ears (% correct)	44.9 ± 22.9 (44) 50.0 (35.0) [0.0,83.0]

Note. Data presented as % (n/N) or as Mean ± *SD (N) Median (Interquartile)* [Range].

D. Safety and Effectiveness Results

a. Safety Results

The safety analysis was based on adverse device effects (ADEs) in the intent-to-treat (ITT) population of 44 participants up to 12 months post-activation. Table 4 below shows the safety outcomes for this study. Table 5 lists the type and number of ADEs.

Table 4: Summary of ADE Classifications

Classification of ADE	Subjects Affected
Number of subjects with any ADE	31/44 (70.5%)
Number of subjects with any serious ADE	21/44 (47.7%)
Number of subjects with any unanticipated ADE	3/44 (6.8%)
Number of subjects with any unanticipated, serious ADE	0/44 (0.0%)

Note. Data presented as *n/N (%).*

Table 5: Type and Number of ADEs

ADE	Number of ADEs	Subjects Affected
ADE type		
Loss of residual hearing	21	47.7% (21/44)
Temporary loss of hearing	7	15.9% (7/44)
Imbalance, dizziness, vertigo	4	9.1% (4/44)
Tinnitus, ringing, beeping	2	4.5% (2/44)
Other surgical complication	1	2.3% (1/44)
Other	3	6.8% (3/44)

Note. Data presented as % *(n/N).*

No subjects experienced an unanticipated, serious ADE or withdrew from the study due to an ADE. Thirteen subjects experienced non-serious ADEs including temporary hearing loss, tinnitus, vertigo, and other surgical or device effects. Serious ADEs included one subjects hospitalized for vertigo and 21 subjects with permanent loss of residual hearing. All subjects with loss of residual hearing were intervened with cochlear implant programming.

The change in hearing thresholds from baseline to 6 months after activation was calculated using the HEARRING Classification Scale (Skarzynski et al., 2013). Table 6 below shows the number and percent of participants with complete, partial, minimal, and no hearing preservation based on a low-frequency pure-tone average from 125-1000 Hz. Of the 43 participants with endpoint data, 27 (62.8%) had complete or partial hearing preservation six months after activation.

Table 6: HEARRING Classification Scale Results at 6 months

Classification	Subjects
Complete Hearing Preservation (> 75%)	3/43 (7.0%)
Partial Hearing Preservation (25-75%)	24/43 (55.8%)
Minimal Hearing Preservation (< 25%)	4/43 (9.3%)
No Hearing Preservation (no detectable hearing)	12/43 (27.9%)

Note. Data presented as *n/N (%).*

Table 7 and Table 8 below show other ways to define hearing preservation. Table 7 is based on the Vienna Consensus, developed in 2023 by 24 surgeons from different countries at a meeting of surgical advisors. The Vienna Consensus defines hearing preservation based on the shift in average low-frequency hearing at 250, 500, and 1000 Hz. Complete hearing preservation means that low-frequency hearing changed 15 dB HL or less. Partial hearing preservation means that hearing changed 16-30 dB HL and complete hearing loss means that hearing changed more than 30 dB HL. Table 8 shows the degree (i.e., normal, mild, moderate, moderately-severe, severe, and profound) of low-frequency hearing loss before surgery and six months after surgery based on LFPTA from 125-1000 Hz.

Table 7: Vienna Consensus Results at 6 months

Classification	Subjects
Complete Hearing Preservation (≤ 15 dB HL)	3/42 (7.1%)

Partial Hearing Preservation (16-30 dB HL)	17/42 (40.5%)
Complete Hearing Loss (> 30 dB HL)	22/42 (52.4%)

Note. Data presented as *n/N (%)*.

Table 8: Degree of Low-Frequency Hearing Loss

Classification	**Pre-Operative**	**Post-Operative**
Normal (LFPTA ≤ 25 dB HL)	0/42 (0.0%)	0/42 (0.0%)
Mild (LFPTA of 26-40 dB HL)	3/42 (7.1%)	0/42 (0.0%)
Moderate (LFPTA of 41-55 dB HL)	10/42 (23.8%)	0/42 (0.0%)
Moderately-Severe (LFPTA of 56-70 dB HL)	17/42 (40.5%)	1/42 (2.4%)
Severe (LFPTA of 71-90 dB HL)	11/42 (26.2%)	13/42 (31.0%)
Profound (LFPTA > 90 dB HL)	1/42 (2.4%)	28/42 (66.7%)

Note. Data presented as *n/N (%)*.

b. Effectiveness Results

The effectiveness analysis was based on data available from 43 subjects at six months post-activation. Table 9, Table 10, and Table 11 below show effectiveness outcomes relative to the study endpoints.

Table 9: Primary Effectiveness Endpoints Results

Outcome Measure	**Baseline (% correct)**	**6 Months (% correct)**	**Change (%)**	***p* value**
CNC Words in quiet, implant ear	26.5 ± 12.4 (44) [10.0,48.0]	52.0 ± 19.9 (43) [4.0,92.0]	25.6 ± 22.8 (43) [-38.0,82.0]	< .01
AzBio Sentences in noise, implant ear	23.5 ± 17.3 (44) [0.0,67.0]	47.0 ± 22.8 (43) [0.0,92.0]	24.1 ± 25.3 (43) [-49.0,86.0]	< .01

Note. Data presented as Mean ± *SD (N)* [Range].

Mean scores on CNC Words in quiet and AzBio Sentences in noise improved in the implant ear alone at six months post-activation compared to baseline. Mean scores at 12 months post-activation continued to show improvement over baseline scores for both CNC Words and AzBio Sentences. In a poolability analysis of between study sites, ANOVA models did not show a significant difference for change in CNC and AzBio scores (p = .35 and .06, respectively).

Table 10 below shows the number and percentage of participants with “better,” “similar,” and “worse” scores on CNC Words in quiet and AzBio Sentences in noise with the cochlear implant six months after activation compared to baseline in the implant ear alone. Scores labeled as “better” were defined as an increase of 10 percentage points or more, which is considered clinically significant. “Similar” scores were within 10 percentage points of baseline, and “worse” scores dropped by more than 10 percentage points.

Table 10: Speech Perception Results at 6 months, Implant Ear Alone

Outcome Measures	**Better**	**Similar**	**Worse**
CNC Words in quiet	38/43 (88.4%)	1/43 (2.3%)	4/43 (9.3%)

AzBio Sentences in noise	31/43 (72.1%)	10/43 (23.3%)	2/43 (4.7%)

Note. Data presented as *n/N (%).*
Better = increase of 10 percentage points or more
Similar = change of less than 10 percentage points
Worse = decrease of 10 percentage points or more

Table 11: Secondary Effectiveness Endpoints Results

		6 months post-activation	
Outcome Measures	**Baseline Score**	**Scores**	**Change**
AzBio Sentences in Noise (+10 dB SNR): everyday listening condition			
Better		60.5% (26/43)	
Similar		20.9% (9/43)	
Worse		18.6% (8/43)	
APHAB: Ease of Communication	59.7 ± 23.2 (43) [18.7,99.0]	30.6 ± 22.4 (42) [1.0,77.0]	-28.8 ± 21.5 (41) [-80.7,16.7]
APHAB: Background Noise	74.4 ± 16.0 (43) [29.0,99.0]	45.7 ± 18.2 (42) [17.2,87.0]	-29.2 ± 23.4 (41) [-70.5,30.5]
APHAB: Reverberation	75.7 ± 16.2 (43) [41.7,99.0]	46.1 ± 18.7 (42) [14.6,85.0]	-30.3 ± 22.7 (41) [-74.7,29.0]
APHAB: Aversiveness	41.2 ± 23.5 (43) [1.0,87.0]	42.0 ± 25.3 (42) [1.0,99.0]	2.2 ± 36.9 (41) [-59.8,92.5]
APHAB: Global Score	69.9 ± 15.6 (43) [40.2,98.3]	40.7 ± 16.9 (42) [16.5,76.0]	-29.5 ± 19.2 (41) [-71.2,4.2]
SSQ: Speech Hearing	2.5 ± 1.5 (43) [0.0,6.3]	4.9 ± 2.0 (42) [1.5,7.7]	2.4 ± 1.9 (41) [-2.9,6.3]
SSQ: Spatial Hearing	3.2 ± 1.8 (43) [0.4,7.4]	4.8 ± 2.1 (42) [0.8,8.6]	1.6 ± 2.3 (41) [-1.9,6.6]
SSQ: Qualities of Hearing	4.4 ± 1.6 (43) [0.4,7.3]	6.1 ± 1.5 (42) [1.2,8.6]	1.7 ± 2.0 (41) [-2.2,6.3]
SSQ: Overall	3.4 ± 1.4 (43) [0.5,6.1]	5.3 ± 1.7 (42) [1.4,7.9]	1.9 ± 1.9 (41) [-1.4,5.7]

Note: Data presented as % (n/N) or as Mean ± *SD (N)* [Range].

Table 11 above shows results of the secondary effectiveness endpoints at six months after activation. Twenty-six subjects (60.5%) were categorized as “better,” and nine subjects (20.9%) categorized as “similar” for AzBio sentences in the everyday listening condition at six months post-activation compared to baseline. Eight subjects (18.6%) were categorized as “worse” for AzBio sentences in the everyday listening condition at six months post-activation compared to baseline. Of these eight subjects, six (75.0%) had a better CNC word score at six months. One subject had was categorized as “worse” at 6 months post-activation on all three testing conditions at six months post-activation.

The mean change of the APHAB Global Score (Cox & Alexander, 1995) from baseline to six months post-activation indicated subjects received benefit from the device, but such changes were not statistically significant (due to the confidence intervals including a score of zero). Mean scores were also improved at six months post-activation for the APHAB subscales for Background Noise, Ease of Communication, and Reverberation. The mean score was similar between baseline and six months post-activation for the APHAB subscale for Aversiveness. Finally, although the mean total score for the Speech, Spatial, and Qualities of Hearing Scale and the overall scale (SSQ; Gatehouse & Noble, 2004) indicated improvements, they did not reach statistical significance at six months post-activation compared to baseline.

c. Pediatric Extrapolation
In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Subgroup Analyses

The study was not specifically powered to examine associations among all baseline characteristics. Post-hoc subgroup analyses were further performed to determine potential associations between baseline characteristics and effectiveness outcomes. Statistical analyses involved multiple linear regression to evaluate the association of sex, implanted ear, race, ethnicity, age, baseline air-conduction thresholds, and baseline speech perception scores. Effectiveness outcomes included CNC Words in quiet (implant ear alone), AzBio Sentences in noise (implant ear alone), and AzBio Sentences in noise in the everyday listening condition (both ears), and the effectiveness endpoint was six months post-activation. When multiple baseline characteristics showed a significant association with effectiveness outcomes ($p<0.05$), they were analyzed with a multiple regression model to control for other factors.

Effectiveness outcomes on CNC, AzBio (implanted ear), and AzBio (both ears) were not significantly different at 3-, 6-, or 12-months post-activation based on sex (male/female) or implanted ear (right/left). A significant difference between white and non-white races on AzBio (implant ear alone) at three months and AzBio (both ears) at three and six months was no longer significant by 12 months post-activation. While ethnicity showed no significant differences on effectiveness outcomes at $p<0.05$, participants with unknown ethnicity showed less improvement on an absolute basis. The single subject with Hispanic/Latino ethnicity had outcomes on CNC at least as good as the non-Hispanic/Latino subjects on an absolute basis. No significant differences were seen on CNC, AzBio (implanted ear), or AzBio (both ears) based on age group at three or six months (effectiveness endpoint) post-activation. Participants over 75 years old showed less improvement on CNC Words at 12 months post-activation, but when change from baseline to six months on CNC, AzBio (implanted ear) and AzBio (both ears) were regressed against age, entered as a continuous variable, age did not show a significant association with these outcomes.

The mean of baseline air-conduction (AC) thresholds at ≤1.0 kHz and baseline CNC Word score were significantly associated with change in CNC score from baseline to six months when evaluated in simple linear regression. A multiple regression model including both mean baseline AC thresholds at ≤1.0 kHz and baseline CNC Word score continued to show an association between baseline AC thresholds at ≤1.0 kHz and CNC at six months post-activation. Multiple regression models also continued to show associations with change in CNC at six months post-activation for participants of unknown ethnicity when the models included combinations of baseline CNC score, Hispanic/Latino ethnicity, and baseline AC thresholds at ≤1.0 kHz.

Overall, there is no evidence that demographic factors are associated with the outcomes of this trial. A

participant's baseline air-conduction thresholds at lower frequencies and baseline CNC Word scores are associated with effectiveness outcomes. However, the R-squared values for the regressions suggest that while these factors provide information for predicting outcomes, they explain a relatively small proportion of the subject-to-subject variability in outcome.

The Applicant's Claims Based on G170111

The tabulated summary below lists all performance statements/claims the Applicant proposed based on study findings from G170111:

Claim #1:	Nearly all MED-EL cochlear implant users (39/43, 90.7%) score better on at least one speech test in their implanted ear alone by 6 months after fitting, based on CNC Words in quiet and AzBio Sentences in noise.
	Many MED-EL cochlear implant users (26/43, 60.5%) score better in their everyday listening condition (using both ears) by 6 months after fitting, based on AzBio Sentences in noise.
Claim #2:	Average speech understanding scores in quiet and in noise double in the implant ear alone 6 months after receiving a MED-EL cochlear implant, improving by 26 percentage points on CNC word score and 24 percentage points on AzBio sentence score.
Claim #3:	Most MED-EL cochlear implant users (78-85%) say that communication in challenging settings is easier with the cochlear implant 6 months after surgery compared to their hearing aids before surgery, based on the APHAB Background Noise (32/41, 78.0%) and Reverberation subscales (35/41, 85.4%) and the SSQ Speech Hearing subscale (32.41, 78%).
	Most MED-EL cochlear implant users (33/41, 80.5%) say they strain less to communicate with the cochlear implant 6 months after surgery compared to their hearing aids before surgery, based on the Ease of Communication subscale on the APHAB.
Claim #4:	Many MED-EL cochlear implant users (24/41, 58.5%) say that speech, music, and everyday sounds are more natural, clear, and easier to identify with the cochlear implant 6 months after surgery compared to their hearing aids before surgery, based on the SSQ Qualities of Hearing subscale scores.
	Many MED-EL cochlear implant users (29/41, 70.7%) say that hearing in the everyday world is easier with the cochlear implant 6 months after surgery compared to their hearing aids before surgery, based on overall SSQ scores.
Claim #5:	Many MED-EL cochlear implant users (20/42, 47.6%) have complete or partial hearing preservation with MED-EL's longer electrodes (FLEX28 and FLEXSOFT) 6 months after surgery, including 3 users with complete hearing preservation (low-frequency shift of 15 dB HL or less) and 17 users with partial hearing preservation (low-frequency shift of 16-30 dB HL).
Claim #6:	Most patients (18/22, 81.8%) without hearing preservation score better on at least one speech test in the implanted ear alone 6 months after surgery, based on CNC Words in

	quiet and AzBio Sentences in noise.
	Many patients (14/22, 63.6%) without hearing preservation understand speech in noise better in the everyday listening condition (using both ears) 6 months after surgery, based on AzBio Sentences.
Claim #7:	The majority – more than half – of MED-EL cochlear implant users (22/41, 53.6%) continue to have aidable hearing in the implant ear with a long FLEX electrode array (28 or 31 mm) 6 months after surgery.
	Aidable hearing is defined by the capabilities of the acoustic unit in the MED-EL system, which can provide gain for thresholds ≤80 dB HL at 125-1000 Hz).

2. Residual Hearing Preservation:

The applicant proposed several claims/performance statements for the MED-EL Cochlear Implant System with FLEX electrode series. Claims #1-#5 are based on RWE collected from MED-EL Hearing Solutions (MEHS) Registry Database and Claim #6 based on non-clinical data collected from four temporal bone studies. The data used to support these claims/ performance statements are presented below.

A. Real-World Evidence from the MEHS Registry Database

The applicant uses RWE in accordance with the FDA Guidance "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" (issued August 31, 2017) to capture post-cochlear implantation hearing preservation outcomes in subjects who are unilateral or bilateral users of MED-EL CIs.

The applicant conducted a prospectively designed, retrospective, multi-centric, retrospective analysis with intra-subject controls from the MEHS registry to capture the residual hearing status 12 to 24 months after implantation among patients implanted with the MED-EL Cochlear Implant System. Data from this analysis, as well as supporting safety and effectiveness evidence from the literature review, were the basis for the PMA approval decision for the applicant's proposed claims on the HP rates for the MED-EL Cochlear Implant System with FLEX electrode series.

The analysis focuses on the FLEX20, FLEX24, FLEX26, FLEX28, and FLEXSOFT electrodes from the MED-EL portfolio attached to the SYNCHRONY, SYNCHRONY 2, MED-EL CONCERT, SONATA, or PULSAR implant housings. The analysis was performed on the 2021-22 extraction of all subjects enrolled in the MEHS registry who were implanted with a FLEX-type electrode and for whom PTA air-conduction thresholds were available both pre- and post-surgery. The following key inclusion and exclusion criteria were used to sort the data and to gain the analytic population:

a. Inclusion Criteria

- Unaided PTA measured by air conduction
- Pre-operative (baseline) assessment at maximum 12 months before surgery
- Post-operative assessment between 6 and 36-months after surgery
- Availability of longitudinal data to allow for the analyses of pre- to post-operative intra-individual changes

- Availability of electrode array type
- Availability of frequencies mandatory for calculation of the hearing preservation scales

b. Exclusion Criteria

- Non FLEX-type electrodes
- Double data entries
- For analysis of low-frequency PTA by American Academy of Otolaryngology (AAO) Scale: pre-operative thresholds ≥80 dB HL
- For analysis of low-frequency PTA by Vienna Consensus Scale: pre-operative thresholds ≥111.67 dB HL (average maximum output levels of the audiometers at 250, 500, and 1000Hz)

This analysis investigated prospectively collected and anonymized data of subjects with a MED-EL CI System as collected in a clinical routine setting as RWE. The RWD were pooled from 4 clinics in Germany (Munich, Heidelberg, Frankfurt, and Oldenburg).

Two approaches for assessing hearing preservation were implemented:

1. AAO standards for functional residual hearing (see Adunka et al., 2018)
2. Vienna Consensus protocol (*Vienna 10 Feb. 2023*).

These two approaches use different frequencies for assessing low-frequency PTA3 (LFPTA3) from 125, 250, and 500 Hz (AAO), and LFPTA3 from 250, 500, and 1000 Hz (Vienna Consensus). The AAO standards are designed to consider the functionality of residual hearing post-implantation and the Vienna Consensus provides guidance for categorizing residual hearing post-implantation. Thus, the MEHS registry analysis is summarized as is follows:

1. Post-op LFPTA3 $_{125, 250, 500\ Hz}$ and individual frequencies at 125; 250; 500; 750; 1000; 1500; 2000; 3000; 4000; 6000; and 8000 Hz in those with pre-op functional hearing in LFPTA3 $_{125, 250, 500\ Hz}$ using the tiered approach according to Adunka et al. 2018, also referred to as AAO-scale. This scale uses a cut-off of <80 dB HL for functional hearing that can be fit with acoustic amplification in the implanted ear.

2. Pre- to post-op changes in low-frequency LFPTA3 $_{250, 500, 1000\ Hz}$ in those with some residual hearing below the audiometer maximum at these frequencies (≤111.7dB HL), also referred to as Vienna Consensus protocol. This scale uses a cut-off of ≤30 dB HL and >15 dB HL change from pre- to post-op for partial hearing preservation, and ≤15 dB HL for complete hearing preservation.

The applicant's proposed HP claims are based on the analysis of the 2021-22 extraction, and was of exploratory nature; assessed data were analyzed and reported descriptively. A summary of the registry design and endpoints is outlined below:

Table 12: Summary of the MEHS Registry Design and Endpoints

Analysis	**Hearing Preservation upon cochlear implantation with MED-EL devices**
Test intervals	According to the local clinical routine, this registry evaluated data as derived from the following time points if available: **Baseline** (pre-implant status or pre-activation status depending on what is available), **Immediately post-implant** (max 3 months from the chosen baseline point), **Post-implant at 6 months** (more than 3 months and less than 1 year from the chosen baseline point) **Post-implant at 1 year** (more than or equal to 1 year and less than 2 years from the chosen baseline point), **Post-implant at 2 years** (more than or equal to 2 years and less than 3 years from the chosen baseline point)
Statistical considerations	The data of the data analysis were analyzed according to the Statistical Analysis Plan. **Data Analysis Hypothesis or Pass/Fail Criteria** Due to the exploratory nature of this data analysis, no hypotheses or pass/fail criteria were defined. Sample Size Calculation All subjects 1) enrolled in the MEHS registry and 2) fulfilling the selection criteria for this data analysis at the selected sites were analyzed. Due to the exploratory nature of this data analysis, no a-priori sample size was calculated. **Statistical Analysis Methods** Descriptive statistics were used to report subject characteristics and to provide a summary of the examined study outcomes. Quantitative data are presented as mean with standard deviation (SD) and / or median with range (minimum and maximum); qualitative data are presented as absolute and relative frequencies.

c. Accountability of Study Cohort

Data came from an extraction of the MEHS registry and completed between February and April 2021 from 4 different clinics in Germany (Klinikum Großhadern München, University Hospital Frankfurt, Evangelisches Krankenhaus Oldenburg; Universitätsklinikum Heidelberg), and an extraction completed by 28th June 2022 from 3 different clinics in Germany (Klinikum Großhadern München, University Hospital Frankfurt, Evangelisches Krankenhaus Oldenburg). Patients consented prior to enrollment.

d. Study Population Demographics and Baseline Parameters

Following the inclusion and exclusion criteria for the HP analysis, data provided unaided PTA assessments in 704 individuals or 968 ears, including 264 bilateral implantees. These data were extracted from users of FLEX20, FLEX24, FLEX26, FLEX28, and FLEXSOFT electrodes. From the initial data selection, 96 ears (86 persons) had frequency responses for 250, 500, 1000 Hz to comply with the LFPTA3 from the AAO scale; and 122 ears (115 persons) had frequency responses for 250, 500, 1000 Hz to comply with the LFPTA3 from the Vienna Consensus were included.

Table 13: MEHS Registry Population Demographics

	AAO		**Vienna**	
Demographics	**n**	**%**	**n**	**%**
Participants	86		115	
ears	96		122	
bilaterally implanted	10		7	
Gender				
female	48	56%	69	60%
male	38	44%	46	40%
other	0	0%	0	0%
Ear to be implanted				
left	47	49%	65	53%
right	49	51%	57	47%
Age	years		years	
median	59.4		59.0	
mean	59.7		58.9	
SD	13.6		16.3	
minimum	30.6		6.4	
maximum	85.1		85.1	

e. Summary of Hearing Preservation Results

AAO Standards:
For this analysis, LFPTA3 for 125, 250 and 500 Hz was calculated (Adunka et al. 2018). Forty-six subjects with data between 12- and 24-months post-implantation that had a pre-operative LFPTA3 <80 dB HL (considered functional hearing), were included for analysis. Between 12- and 24-months post-implantation, 90% of the FLEX24, 100% of the FLEX26, 55% of the FLEX28, and 8% of the FLEXSOFT patients maintained an LFPTA3 <80 dB HL.

Vienna Consensus:
For the analysis according to the Vienna Consensus, LFPTA3 at 250, 500, and 1000 Hz was categorized by the amount of shift experienced at various time points post-operatively. Fifty-four subjects with data between 12- and 24-months post-implantation were included for analysis. At this timepoint, 75% of FLEX24 recipients, 50% of FLEX26 recipients, 62% of FLEX28 recipients, and 44% of FLEXSOFT recipients maintained a shift in LFPTA3 ≤ 30 dB HL.

- Of the eight FLEX24 recipients, 38% maintained a shift in LFPTA3 ≤ 15 dB HL, and 38% maintained a shift in LFPTA3 >15 ≤ 30 dB HL, thus 75% ≤ 30 dB HL.

- Of the two FLEX26 recipients, 50% maintained a shift in LFPTA3 ≤ 15 dB HL, and 0% maintained a shift in LFPTA3 >15 ≤ 30 dB HL, thus 50% ≤ 30 dB HL.

- Of the twenty-six FLEX28 recipients, 27% maintained a shift in LFPTA3 ≤ 15 dB HL, and 35% maintained a shift in LFPTA3 >15 ≤ 30 dB HL, thus 62% ≤ 30 dB HL.

- Of the eighteen FLEXSOFT recipients, 22% maintained a shift in LFPTA3 ≤ 15 dB HL, and 22% maintained a shift in LFPTA3 >15 ≤ 30 dB HL, thus 44% ≤ 30 dB HL.

f. Conclusions

Data from the MEHS registry demonstrated that HP is possible with MED-EL FLEX electrode arrays. Analyzed by two different methods, these data show that many recipients of the MED-EL FLEX electrode arrays demonstrate some degree of HP 12 to 24 months after implantation (57% Vienna Consensus, 52% AAO). As RWE, data contained within the registry reflect clinical practice and evaluate hearing preservation with FLEX electrode arrays in a wide range of patients and several surgeons.

g. Real-World Data (RWD) Quality Analyses

The relevance and reliability of RWD (collected from the above a prospectively designed, retrospective, multi-centric, longitudinal, clinical analysis) were evaluated according to the FDA RWE guidance document. Overall, the RWD are of sufficient quality to ensure the reliability of the RWD source and the validity of the analysis finding to support the proposed HP claims/performance statements #1-#5, with some major data limitations noted in the section below.

h. Limitations for the RWD Analysis

Limitations of the RWD collected from the prospectively-designed, retrospective, multi-centric, longitudinal, clinical analysis include: 1) significant subject attrition rate (e.g., for Vienna consensus analyses, there were n=115 subjects with pre- and post-measurements; at 6 to 12 months, n=95 subjects; at 12 to 24 months, n=54 subjects), which can introduce selection bias; 2) the statistical hypothesis along with the success criterion for the primary endpoint for HP rates was not pre-specified in the analysis protocol, and the HP data were only descriptively analyzed, and 3) long-term HP outcomes beyond 24 months associated with the FLEX series of the MED-EL Cochlear Implant System were not fully captured or absent in the retrospective analysis due to subject attrition during the post-operative follow-up period. Given that the sample size of HP outcomes up to 12-24 months post-implantation based on the Vienna consensus (54 subjects) and the AAO-Adunka et al. 2018 (46 subjects) is equivalent to that of a pivotal study for cochlear implantation, it was thus concluded that the RWD collected from the MEHS registry can be used as main clinical evidence to support the proposed HP claims/performance statements #1-#5.

B. Temporal Bone Studies

Structure preservation is considered a prerequisite for HP, and full scala tympani (ST) insertion of the electrode array is generally recognized as a favorable position to reduce the risk of intracochlear trauma and preserve residual hearing.[1] Both scala vestibuli (SV) insertion and electrode translocation between scalae are widely recognized as introducing intracochlear trauma. Indeed, when damage occurs to the cochlear partition, such as during a translocation, therefore allowing endolymph and perilymph to mix, this scenario is well-recognized as causing a physiologic insult to cochlear neural elements that can damage residual hearing sensitivity. MED-EL conducted temporal bone studies to assess the electrode placement of MED-EL FLEX electrodes and calculate the rate of ST insertion without dislocation into the SV.

a. Methods

Four temporal bone studies assessing cochlear damage after insertion of MED-EL FLEX electrodes (FLEXSOFT, FLEX28, FLEX24 and FLEX20) were analysed, totalling 38 samples. These studies classified

cochlear damage according to Eshraghi 2003[2], with scalar dislocation categorized as Grade 3 (electrode in SV). Rates of ST insertion without dislocation were calculated for each electrode variant and for all electrode variants together.

b. Results
Results of temporal bone experiments are shown in Table 17.

Table 14: Temporal bone studies with MED-EL FLEX electrodes.

	Temporal Bone Studies (n = 4 studies)			
Electrode Array	Temporal bones (n)	G3*: Scala dislocation (n)	% ST dislocation	% ST insertion
FLEXSOFT	5	1	20,0	80,0
FLEX28	8	0	0,0	100,0
FLEX 24	15	0	0,0	100,0
FLEX20	10	0	0,0	100,0
Total	**38**	**1**	**2,6**	**97,4**

*Grade 3 (electrode in SV) based on Eshraghi 2023.

Four temporal bone studies were included in the analysis for a total of 38 samples (FLEXSOFT [n = 5], FLEX28 [n = 8], FLEX24 [n = 15], and FLEX20 [n = 10]). Only one (n = 1) case of scalar dislocation was observed for the FLEXSOFT electrode. The rate of ST dislocation for all electrodes investigated is 2.6% and the rate of ST insertion is 97.4%.

The rates of ST insertion for the single MED-EL FLEX electrode variants evaluated are the following:
- FLEXSOFT: 80.0% (4 out of 5 temporal bones) scala tympani insertions
- FLEX28: 100.0% (8 out of 8 temporal bones) scala tympani insertions
- FLEX24: 100.0% (15 out of 15 temporal bones) scala tympani insertions
- FLEX20: 100.0% (10 out of 10 temporal bones) scala tympani insertion

c. Conclusion
Data obtained by temporal bone studies demonstrated that MED-EL FLEX electrodes support insertion into ST, without dislocation into SV, in 97.4% of cases. Proper placement into ST is generally considered a favourable outcome for reducing intracochlear trauma risk.

The Applicant's Claims based on RWE (#1-5) and Temporal Bone Studies (#6)

The tabulated summary below lists all performance statements/claims the Applicant proposed based on analysis of RWE and temporal bone studies

Claim #1:	The majority – more than half - of recipients with FLEX electrode arrays (57.4% or 31 out of 54 subjects implanted with FLEX24, FLEX26, FLEX28, and FLEXSOFT) maintain some degree of acoustic residual

	hearing over a period of 12 to 24 months. This is demonstrated by a shift in audiometric thresholds of ≤ 30 dB HL compared to preoperative levels. Fifteen out of 54 recipients (27.8%) had complete hearing preservation, demonstrated by a shift in low-frequency hearing (250 Hz, 500 Hz, 1000 Hz) of ≤ 15 dB HL. Sixteen out of 54 recipients (29.6%) had partial hearing preservation, demonstrated by a shift in low-frequency hearing (250 Hz, 500 Hz, 1000 Hz) between 16- and 30-dB HL.
Claim #2:	Many MED-EL cochlear implant users (31/54 or 57.4%) have some degree of hearing preservation 1-2 years after surgery with FLEX electrodes, as defined by a shift in low-frequency pure-tone average less than or equal to 30 dB HL.
Claim #3:	Some degree of acoustic hearing preservation has been shown in MED-EL cochlear implant users 1-2 years after surgery regardless of electrode array length (57.4%; 31/54) (of patients experienced a shift ≤30 dB HL (250 Hz, 500 Hz, 1000 Hz), 52.2%; 24/46) had a PTA < 80 dB HL (125 Hz, 250 Hz,500 Hz)). Most FLEX24 patients had some degree of hearing preservation (75.0%; 6/8) of patients experienced a shift ≤30 dB HL, 90.0% or 9/10) had a PTA < 80 dB HL). Many FLEX26 patients had some degree of hearing preservation (50.0%; 1/2) of patients experienced a shift ≤30 dB HL, 100.0%; 2/2) had a PTA < 80 dB HL). Many FLEX28 patients had some degree of hearing preservation (62.0%; 16/26) of patients experienced a shift ≤30 dB HL, 54.5% (12/22) had a PTA < 80 dB HL). Some FLEXSOFT patients had a degree of hearing preservation (44.0%; 8/18) of patients experienced a shift ≤30 dB HL, 8.3% (1/12) had a PTA < 80 dB HL).
Claim #4:	Many recipients of MED-EL FLEX electrodes between 24 and 31.5 mm in length continue to have complete or partial hearing preservation a year after surgery, as defined by a shift in low-frequency hearing less than or equal to 30 dB HL (250 Hz, 500 Hz, 1000 Hz) (31 of 54 or 57.4%) and a PTA less than 80 dB HL (125 Hz, 250 Hz, 500 Hz) (24 of 46 or 52.2%). Fifteen of 54 recipients (27.8%) had complete hearing preservation (shift ≤15 dB HL) a year after receiving a MED-EL FLEX electrode array. Sixteen of 54 recipients (29.6%) had partial hearing preservation (shift 16-30 dB HL) a year after receiving a MED-EL FLEX electrode array.

Claim #5:	When changes to post operative hearing levels are monitored over time, many patients have outcomes categorized as 'preserved hearing,' according to the Vienna Consensus protocol, for at least two years after surgery (57.4% or 31 out of 54 subjects monitored in a registry study). Fifteen out of 54 recipients (27.8%) had complete hearing preservation, demonstrated by a shift in low-frequency hearing (250 Hz, 500 Hz, 1000 Hz) of ≤ 15 dB HL. Sixteen out of 54 recipients (29.6%) had partial hearing preservation, demonstrated by a shift in low-frequency hearing (250 Hz, 500 Hz, 1000 Hz) between 16- and 30-dB HL.
Claim #6:	Based on pre-clinical temporal bone studies, the MED-EL FLEXSOFT, FLEX28, FLEX24, and FLEX20 electrode designs support insertion into the scala tympani in 97.4% of cases (37 out of 38 temporal bones), without translocating into scala vestibuli, which is generally considered a favourable outcome for reducing intracochlear trauma risk. • FLEXSOFT: 80.0% (4 out of 5 temporal bones) scala tympani insertions • FLEX28: 100.0% (8 out of 8 temporal bones) scala tympani insertions • FLEX24: 100.0% (15 out of 15 temporal bones) scala tympani insertions • FLEX20: 100.0% (10 out of 10 temporal bones) scala tympani insertion

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal IDE clinical study included 61 investigators of which 0 were full- time or part-time employees of the sponsor and 5 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 5
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

The principal Investigators of the involved clinics of the MEHS registry have adequately disclosed their financial interest/arrangements with the sponsor.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Systematic Literature Review to Support HP Claims #1-5

a. Literature Search Strategy

MED-EL conducted a systematic literature review to collect supporting evidence for the HP claims #1-5 for MED-EL FLEX electrodes. While the details of these claims (i.e., percentages, ratios) are based on the data from the RWE, the following provides additional supporting evidence. Please note approval of these claims was entirely based on the RWE. The search terms and inclusion/exclusion criteria are listed in Table 17, and the appraisal criteria are listed in Table 18 below.

Table 15: Combinations of Search Terms for PubMed search

Search Step	**Search Terms**	**# of retrieved publications**
1	cochlear implant	16227
2	(hearing preservation) OR (residual hearing)	4300
3	1 AND 2	1188
4	Limit 3 to 10 years (literature search was conducted on November 07, 2019)	841
Inclusion Criteria		
Population, disease, or condition	Cochlear implantees	
Intervention or treatment	Cochlear implant	
Comparator	None	
Outcomes	Hearing preservation	
Exclusion Criteria		
E1	Publication lacking sufficient information	
E2	Not a clinical study in human	
E3	Case series with too small sample size (< 5)	

Search Step	**Search Terms**	**# of retrieved publications**
1	cochlear implant*	19963
2	(hearing preservation) OR (residual hearing)	6736
3	1 AND 2	1708
4	Limit 3 to Publication dates: August 16, 2019 to February 28, 2022	322
5	Limit 4 to Languages: English and German	316
Inclusion Criteria		
Population, disease, or condition	Cochlear implantees	
Intervention or treatment	Cochlear implant	

Comparator	None
Outcomes	Hearing preservation
Exclusion Criteria	
E1	Not a clinical study in human
E2	No FLEX electrode used
E3	Publication lacking sufficient information
E4	Case study or case series with too small sample size (< 5)
E5	The publication has been published in the previous search period

Table 16:- Literature Appraisal Criteria

Data Suitability	**Description**	**Grading System**
Appropriate Device	Where the data generated from the device in question?	D1 – Actual device
		D2 – Comparable device
		D3 – Other device
Appropriate Device Application	Was the device used for the same intended use (e.g. methods of deployment, application, etc.)?	A1 – Same use
		A2 – Minor deviation
		A3 – Major deviation
Appropriate Patient Group	Were the data generated from a patient group that is representative of the intended treatment population (e.g. age, sex, etc.) and clinical condition (i.e. disease including state and severity)?	P1 – Applicable
		P2 – Limited
		P3 – Different population
Acceptable Report/Data Collation	Did the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 – High quality
		R2 – Minor deficiencies
		R3 – Insufficient information
Data Contribution	**Description**	**Grading System**
Data Source Type	Was the design of the study appropriate?	T1 – Yes
		T2 – No
Outcome Measures	Did the outcome measures reported reflect the intended performance of the device?	O1 – Yes
		O2 - No
Follow-Up	Was the duration of the follow-up long enough to assess treatment effects and identify complications?	F1 – Yes
		F2 - No
Statistical Significance	Was a statistical analysis of the data provided and appropriate?	S1 – Yes
		S2 - No
Clinical Significance	Was the magnitude of the treatment effect observed clinically significant?	C1 – Yes
		C2 - No

b. Results of the Systematic Literature Search on Hearing Preservation

i. Functional Hearing

Twelve studies (de Carvalho 2013, Guimaraes 2015, Helbig 2018, Helbig 2011, Lenarz 2019, Hollis 2021, Jensen 2021, Masood 2020, Pillsbury 2018, Thompson 2020, Usami 2011 and Usami 2014) defined the presence of low-frequency pure-tone averages (LF-PTAs) less than 80, 85 or 90 dB, or eligible for EAS as successful HP. Raw audiogram data was available from two additional studies (Erixon 2015 and Mahmoud 2014) to enable the determination of post-operative hearing preservation. All studies had pre-operative criteria for functional hearing and used FLEXEAS, FLEX28, and FLEXSOFT electrodes. Successful HP rates ranged from 53% to 100% among the studies, with each author using one of the scales mentioned above to define hearing preservation (LFPTA of less than 80, 85, or 90 dB or eligible for fitting EAS, depending on the study). While each study used slightly different criteria to define functional hearing (i.e., aidable hearing) after implantation, the criteria used are similar enough to draw a broad conclusion that functional hearing after implantation is achievable across studies.

Looking at the criterion of a LFPTA ≤ 80 dB specifically, which closely aligns with the Adunka/AAO scale, seven studies (de Carvalho 2013, Erixon 2015, Guimaraes 2015, Lenarz 2019, Mahmoud 2014, Hollis 2021 and Masood 2020) used a LFPTA of ≤ 80 dB to define functional hearing after implantation. Eighty-one ears were tested. FLEXEAS was the most-used electrode, while two studies (Hollis 2021 and Masood 2020), used FLEX28 and FLEXSOFT. The rates of achieving functional hearing ranged from 57% to 100% among the studies with a median rate of 89%. Five studies with 56 ears had a follow-up of at least one year. Functional HP rates ranged from 29% to 100% among these studies with the median rate of 89% at least one year after surgery, as measured using a LFPTA of ≤ 80 dB mentioned above.

ii. Pre-to-post-operative changes in LFPTAs

A LFPTA shift of 30 dB was used as a cut-off to define complete or partial hearing preservation in ten studies (Bruce 2014, Haumann 2019, Helbig 2016, Helbig 2011, Lenarz 2019, Nordfalk 2016, Pillsbury 2018, Rajan 2012, Suhling 2016 and Matin 2021) including 458 subjects. The rates of achieving complete or partial HP among these studies ranged from 52% to 85% with a median rate of 70%. Among seven studies (Bruce 2014, Helbig 2011, Helbig 2016, Pillsbury 2018, Rajan 2012, Suhling 2016 and Matin 2021), with a follow-up of at least 12 months in 300 FLEX electrode recipients, the HP rate ranged from 49% to 83% with a median value of 68%. Four studies (Haumann 2019, Lenarz 2019, Suhling 2016 and Matin 2021) used pre- to post-operative PTA shift of 15 dB as cut-off for complete HP. The complete HP rate ranged from 10% to 83%. Complete HP at 12 months was reported by Suhling 2016 and Matin 2021 with a HP rate of 40% and 21% respectively.

c. Conclusions from the Systematic Literature Search supporting the HP Claims

Hearing preservation rates reported in the literature vary according to the definition used to capture these outcomes, as well as other surgical or patient factors. Studies defining functional HP as a LFPTA less than 80, 85, or 90 dB or by the ability to use electric-acoustic stimulation demonstrated that functional hearing rates ranged from 53% to 100%. Studies specifically using a LFPTA cut-off of less than 80 dB had a median HP rate of 89%. Studies using a LFPTA shift of less than 30 dB to define complete or

partial HP showed an HP rate of 52% to 85% with a median HP rate of 70%. Taken together, this literature supports the ability to preserve some degrees of low-frequency hearing across a wide range of patients when using FLEX electrode arrays.

B. Systematic Literature Search To Support HP Claim #6

a. Literature Search Strategy

MED-EL performed a systematic literature review for non-clinical data to support the rate of ST insertion of MED-EL FLEX electrode arrays identified in temporal bone studies (Claim #6). While the approval of this this claim is based on the data generated from the temporal bone studies conducted by the applicant, the following provides additional supporting evidence. The search terms and inclusion/exclusion criteria used are listed in Table 20, and the appraisal criteria are listed in Table 21 below. Note that intentional insertion into the SV is excluded. An intentional insertion into the SV is recognized as less than optimal and is typically attempted only when anatomical barriers preclude ST insertion, for example in cases of cochlear ossification.

Table 17: Search Terms, Inclusion and Exclusion criteria for Scalar Position of Electrode Arrays

Database: PubMed		
Search Step	**Search Terms**	**# of retrieved publications**
1	cochlear implant*	15498
2	scala vestibuli	463
3	scala tympani	1403
4	2 OR 3	1515
5	1 AND 4	623
6	Limit 5 to *Publication dates*: 5 years (literature search was conducted on August 13, 2019)	160
7	Limit 6 to *Species*: Humans	108
8	Limit 7 to *Languages*: English	106
Inclusion Criteria		
Population, disease, or condition	Cochlear implantees	
Intervention or treatment	Cochlear implant	
Comparator	No restriction	
Outcomes	Scalar dislocation	
Exclusion Criteria		
E1	Scala vestibuli insertion is planned due to cochlear abnormality (e.g. ossification)	
E2	Device with unspecified product name or type name	
E3	Publication lacking sufficient information	

E4	Cadaveric study
E5	Case report

Database: PubMed

Search Step	Search Terms	# of retrieved publications
1	cochlear implant*	20032
2	scala vestibuli OR scala tympani	1643
3	scalar deviation OR scalar dislocation OR scalar translocation OR scalar location or scalar position	1130
4	2 OR 3	2710
5	1 AND 4	832
6	Limit 5 to *Publication dates*: August 12, 2019 to February 28, 2022	107
7	Limit 6 to *Languages*: English and German	105

Inclusion Criteria	
Population, disease, or condition	Cochlear implantees
Intervention or treatment	Cochlear implant
Comparator	No restriction
Outcomes	Scalar dislocation
Exclusion Criteria	
E1	Scala vestibuli insertion is planned due to cochlear abnormality (e.g. ossification)
E2	Device with unspecified product name or type name
E3	Publication lacking sufficient information
E4	Cadaveric study
E5	Case report

Database: Cochrane

Search Step	**Search Terms**	**# of retrieved publications**
1	cochlear implant*	732
2	scala vestibuli OR scala tympani	12
3	scalar deviation OR scalar dislocation OR scalar translocation OR scalar location or scalar position	22
4	2 OR 3	30
5	1 AND 4 with Cochrane Library publication date from Aug 2014 to Feb 2022	9

Inclusion Criteria	
Population, disease, or condition	Cochlear implantees
Intervention or treatment	Cochlear implant
Comparator	No restriction
Outcomes	Scalar dislocation
Exclusion Criteria	
E1	Not a clinical study in human
E2	No relevant devices used
E3	Publication lacking sufficient information
E4	Case Report or case series of subjects with scalar translocation
E5	Scalar dislocation is not defined as outcome measurement
E6	Publication has been included in previous literature review

Table 18: Literature Appraisal Criteria

Data Suitability	**Description**	**Grading System**
Appropriate Device	Where the data generated from the device in question?	D1 – Actual device
		D2 – Comparable device
		D3 – Other device
Appropriate Device Application	Was the device used for the same intended use (e.g. methods of deployment, application, etc.)?	A1 – Same use
		A2 – Minor deviation
		A3 – Major deviation
Appropriate Patient Group	Were the data generated from a patient group that is representative of the intended treatment population (e.g. age, sex, etc.) and clinical condition (i.e. disease including state and severity)?	P1 – Applicable
		P2 – Limited
		P3 – Different population
Acceptable Report/Data Collation	Did the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 – High quality
		R2 – Minor deficiencies
		R3 – Insufficient information
Data Contribution	**Description**	**Grading System**
Data Source Type	Was the design of the study appropriate?	T1 – Yes
		T2 – No
Outcome Measures	Did the outcome measures reported reflect the intended performance of the device?	O1 – Yes
		O2 - No
Follow-Up	Was the duration of the follow-up long enough to assess treatment effects and identify complications?	F1 – Yes
		F2 - No
Statistical Significance		S1 – Yes

	Was a statistical analysis of the data provided and appropriate?	S2 - No
Clinical Significance	Was the magnitude of the treatment effect observed clinically significant?	C1 – Yes
		C2 - No

b. Results of the Systematic Literature Search

Table 22 provides a summary on the rate of ST insertion and dislocation of MED-EL FLEX electrode arrays (FLEXSOFT, FLEX28, FLEX24) based on 11 publications evaluating scalar positions for MED-EL FLEX electrode arrays. Please note that no published studies addressing scalar dislocation for the FLEX20 electrode variant were identified.

Table 19: Summary of ST insertion rate for MED-EL FLEX electrode arrays from the SLR

	Systematic Literature (n = 11)			
Electrode	MED-EL FLEX electrode recipients (n)	Scala tympani dislocation (n)	% Scala tympani dislocation	% Scala tympani insertion
FLEXSOFT	56	11	19,6	80,4
FLEX28	266	17	6,4	93,6
FLEX 24	43	1	2,3	97,7
FLEX20	NA	NA	NA	NA
Total	**365**	**29**	**7,9**	**92,1**

NA = Not Applicable, because no studies addressing the scalar dislocation rate of FLEX20 were found in the systematic review.

From a total of 11 analyzed publications, where MED-EL FLEX electrode arrays (FLEXSOFT, FLEX28, and FLEX24) were used, intracochlear electrode position was radiologically determined in 365 ears. Scalar translocation and unintended SV insertion occurred in 29 (7.9%) cases in total, resulting in 336 (92.1%) cases with ST insertion. The rate is much higher than a review published by Dhanasingh 2019[1] where a rate of ST insertion of 77.6% or lower, if SV insertion was not counted as scalar translocation, was identified. Dhanasingh 2019 found an incidence rate of 22.4% for scalar translocation, demonstrating that intracochlear trauma caused by scalar translocation is a sometimes-occurring event during cochlear implantation independently of electrode type or manufacturer. The publication showed an incidence rate of 32% for pre-curved electrode array designs and of 6.7% for lateral-wall electrode array designs. The scalar translocation rate of 6.7% for lateral-wall electrodes from the publication is similar to the rate of 7.9% for MED-EL FLEX electrodes, which are exclusively lateral-wall electrodes, obtained from this literature review.

c. Conclusions from the Systematic Literature Search supporting HP Claim #6

Radiographic analysis is an accepted means of quantifying cochlear trauma, especially as it relates to scalar translocation. The results of the systematic review showed a 92.1% ST insertion rate, without dislocation

[1] Dhanasingh A, Jolly C (2019) Review on cochlear implant electrode array tip fold-over and scalar deviation. J Otol 14(3):94–100. https://doi.org/10.1016/j.joto.2019.01.002

into the SV, for MED-EL FLEX electrode arrays (FLEXSOFT, FLEX28, FLEX24, and FLEX20). These results support the 97.4% rate of ST insertion for MED-EL FLEX electrode arrays identified in temporal bone studies (see section above). Therefore, the applicant concludes that MED-EL's flexible electrode arrays are designed to reduce the rate of SV insertion, and the available evidence (i.e., temporal bone studies and systematic literature review) supports this conclusion.

C. Limitations for the Systematic Literature Reviews supporting HP Claims

There were several limitations to the systematic literature review, including: 1) across published studies a variety of HP/histological outcome measurements were used. This makes it challenging to summarize findings across studies, and precludes statistical meta-analyses on the literature data, 2) other electrode arrays (except for FLEX series) were included in some studies, 3) a number of studies were retrospectively designed; that is, data collection and analyses were not prospectively defined in the study protocol, and 4) complete details regarding HP endpoints, inclusion/exclusion measures, and statistical analysis plan etc., are often not fully specified in the cited published studies. However, the data from the articles identified through the literature search cover all of FLEX series. Therefore, the HP/histological outcomes reported in the literature can serve as confirmatory evidence for the outcomes from the prospectively designed, retrospective, clinical analysis along with temporal bone studies and as supporting evidence for the proposed marketing HP claims #1-#6 according to the FDA Guidance document titled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" (issued August 31, 2017).

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the ENT Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

a. Expanded Indications in the Adult Cochlear Implant Population (IDE #G170111)

For both pre-specified co-primary endpoints in this study, post-implant performance was compared to pre-operative baseline. Performance was measured using the CI alone at six months post-activation and compared to the preoperative, best aided baseline condition in the ear to be implanted. The co-primary effectiveness endpoints were defined as a mean improvement in CNC Words in quiet and AzBio Sentences in noise, respectively. Statistically significant improvements in mean CNC Words in quiet (25.6%, SD = 22.8, $p < .01$) and in mean AzBio Sentences in noise (24.1%, $SD = 25.3$, $p < .01$) occurred from the pre-operative, best-aided baseline in the ear to be implanted to the 6-month post activation with cochlear implant alone condition. It was thus concluded that both co-primary effectiveness endpoints were met.

In addition, the secondary effectiveness endpoint was defined as the number and percentage of subjects with "similar" or "better" (i.e., considered clinically significant) for AzBio sentences in noise at six months after activation compared to baseline in the everyday listening condition. Twenty-six participants (60.5%) scored better, and nine participants (20.9%) showed similar scores on AzBio Sentence in noise

in the everyday listening condition at six months post-activation compared to baseline. Eight participants (18.6%) had a worse AzBio sentence score in the everyday listening condition at six months post-activation compared to baseline.

b. Hearing Preservation Claims (MEHS Data Registry)

Data from the MEHS data registry demonstrated that hearing preservation is possible with MED-EL FLEX electrode arrays. Analyzed by two different methods (i.e., Vienna Consensus, AAO-Adunka et al. 2018), this data shows that many recipients of MED-EL FLEX electrode arrays demonstrate some degrees of hearing preservation 12 to 24 months after implantation. 57.4% (31 out of 54) subjects demonstrate a pre-to-post implant PTA (250 Hz, 500 Hz, and 1000 Hz) shift in audiometric thresholds ≤30 dB HL (Vienna Consensus) and 52% (24 out of 46) subjects have functional hearing defined by AAO-Adunka et al. 2018 (a PTA (125 Hz, 250 Hz, and 500 Hz) < 80 dB HL) 1-2 years after implantation.

c. Systematic Literature Review for Hearing Preservation

The literature data provide supporting evidence of HP for the MED-EL FLEX electrode series. These studies demonstrate that HP is possible with MED-EL FLEX electrodes across different methods of analysis. Depending on the methods used for capturing HP outcomes, HP rate ranges from 29% to 100%. Studies using the method of "functional hearing" (i.e., aidable hearing) and the hearing shift in LFPTA (≤30 dB HLZ) had a median HP rate of 89% and a median HP rate of 68%, respectively, at a follow-up of at least one year after implantation.

d. Temporal Bone Studies and Supporting Literature for Scalar Translocation

The four temporal bone studies conducted by the applicant demonstrated that MED-EL FLEX electrode arrays can be inserted into the ST, without dislocating into the SV, which is generally considered a favorable outcome for reducing intracochlear trauma risk and preserve residual hearing, in 97.4% of cases. The rate of ST insertion for MED-EL FLEX electrodes is supported by additional literature showing a 92.1% rate of ST insertion calculated from 11 publications including 365 MED-EL Cochlear Implant users with FLEX electrode arrays.

B. Safety Conclusions

The risks of the device for the proposed expanded indications for use are based on data collected in the pivotal study (G170111) conducted to support PMA approval as described above. The primary safety objective was to report all complications/adverse events (major or minor complications) as the number of individuals experiencing an adverse event. Thirty-one participants experienced an ADE. Thirteen participants experienced non-serious ADEs including temporary hearing loss, tinnitus, vertigo, and other surgical or device-related events. Serious ADEs included one participant hospitalized for imbalance and 21 participants with permanent loss of residual hearing. About half of subjects (20/42, 47.6%) had complete (3 subjects <15 dB) or partial (17 subjects, 16-30 dB) HP six months after surgery. About half of subjects (22/41, 53.6%) continued to have aidable hearing (PTA≤80 dB HL at 125-1000 Hz) in the implant ear six months after surgery. No participants experienced an unanticipated, serious ADE or withdrew from the study due to an ADE. No deaths, device failures, or revision surgeries occurred during this study.

C. Benefit-Risk Determination

a. Expanded Indications in the Adult Cochlear Implant Population

The probable benefits of the device are primarily based on data collected in the clinical study (G170111) conducted to support PMA approval as described above. The study results for the MED-EL Cochlear Implant System demonstrated a statistically and clinically significant benefit to speech recognition in the CI alone condition six months after implantation for both in quiet and in noise, compared to the pre-operative, best aided performance in the ear to be implanted. In addition, 81.4% of the subjects exhibited similar (20.9%) or better (60.5%) performance on AzBio Sentence in noise in the everyday listening condition at six months post-activation compared to pre-operative baseline. Therefore, the MED-EL Cochlear Implant System is expected to improve speech recognition (in terms of CNC Words in quiet and AzBio Sentences in noise) for a majority of the indicated, expanded population.

The probable risks of the device are also based on data collected in the clinical study (G170111) conducted to support PMA approval as described above. The safety data from the clinical study suggest that the subjects tolerated the risks well, especially since the majority of adverse events were device/procedure related to cochlear implantation surgery and resolved postoperatively. The observed major and minor complications/adverse events were consistent with those seen among patients who meet the previously approved indication for use, except for loss of residual hearing, an expected risk of implanting patients with more residual hearing in the ear to be implanted. The analysis on post-operative, residual hearing status showed that about half of subjects achieved some degree of HP six months after surgery. Additional factors considered in determining probable risks and benefits for the MED-EL Cochlear Implant System included patient perspectives.

Patient Perspectives

Patient perspectives considered during the review included: subjective measures of benefit and satisfaction. The majority of participants demonstrated improvements in benefit and satisfaction evaluated by both SSQ and APHAB questionnaires. The SSQ showed that 70.7% of participants reported improvement overall, and 78.0% of participants reported improvement on speech hearing and the APHAB showed improvement in 82.9% of participants on the global score and 82.5% of participants on ease of communication with the MED-EL Cochlear Implant System, compared to their hearing aids before surgery.

In conclusion, given the available information above, the data support that the overall benefits of the MED-EL Cochlear Implant System outweigh the risks who have limited benefit from traditional hearing aids and who meet the criteria specified in the proposed indication for use.

b. Hearing Preservation Outcomes

RWD collected from the MEHS Registry Database and literatures provide main and supporting evidence to support that HP is possible for MED-EL FLEX electrode series 12 to 24 months after implantation. The four temporal bone studies demonstrated that MED-EL FLEX electrode arrays can be inserted into ST, without dislocating into the SV in 97.4% of cases. The above data generally support the proposed HP marketing claims.

D. Overall Conclusions

The data from the pivotal study G170111 in this application support a reasonable assurance of safety and effectiveness for this device when used in accordance with the expanded indications for use among

individuals 18 years of age and older with moderate to profound SNHL and limited benefit from appropriately-fit hearing aids in the ear(s) to be implanted. Based on the pivotal clinical study results, it is reasonable to expect clinical benefits with use of the MED-EL Cochlear Implant System in terms of improvement in speech understanding in quiet and noise since the average performance of the study population showed statistically significant improvement in the co-primary effectiveness endpoint measures. The risks associated with implanting the MED-EL Cochlear Implant System are comparable to those seen among patients who meet previously approved indication for use, except for loss of residual hearing, an expected risk of implanting patients with more residual hearing in the ear to be implanted. FDA believes that the available data demonstrate that the benefits outweigh the risks in the pivotal study subject population for the expanded indication for use of the MED-EL Cochlear Implant System. Additionally, RWE collected from the MEHS Registry Database, along with supporting literature generally support that HP is possible for the MED-EL FLEX electrode series 12 to 24 months after implantation.

XV. CDRH DECISION

CDRH issued an approval order on October 3, 2024. The final conditions of approval cited in the approval order are described below.

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

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