DE NOVO CLASSIFICATION REQUEST FOR

MINDER SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Sub-scalp implanted electroencephalogram system for remote patient monitoring**. A sub-scalp implanted electroencephalogram (EEG) system for remote patient monitoring is a prescription device used for continuously acquiring, transmitting, and storing electrical brain activity of patients with epilepsy. The device consists of sub-scalp implanted electrodes that are connected to a transmitter or storage device. The device is used to aid clinicians in the remote monitoring of electrical activity in the patient's brain. The device is not intended to be implanted in brain tissue.

NEW REGULATION NUMBER: 21 CFR 882.1360

CLASSIFICATION: Class II

PRODUCT CODE: SEM

BACKGROUND

DEVICE NAME: Minder System

SUBMISSION NUMBER: DEN240062

DATE DE NOVO RECEIVED: October 18, 2024

SPONSOR INFORMATION:

Epiminder Pty. Ltd.
384-388 Albert Street East
Melbourne VIC 3002
Australia

INDICATIONS FOR USE

The Minder System is indicated as follows:

> "The Minder System is an electroencephalographic (EEG) recording and transmitting device implanted under the scalp. It is a prescription device indicated to acquire, transmit, and store EEGs continuously from patients between 18-75 years of age with drug-resistant epilepsy who are intolerant or not indicated for more conservative monitoring tools. The Minder System is intended to aid in a physician's remote assessment and

monitoring of the indicated patient's condition. Remote patient assessment and monitoring for this use is defined as the patient's EEG data is available for review by a healthcare provider located at a different location from the patient and where the data is being collected.

The medical use of the data acquired by the Minder System is to be performed under the direction and interpretation of a licensed medical professional. The Minder System does not provide any diagnostic conclusions about the patient's condition."

LIMITATIONS

The sale, distribution, and use of the Minder System are restricted to prescription use in accordance with 21 CFR 801.109.

The operational life of the Minder System is 3 years. The operational life is defined as the device being able to acquire, transmit, and store clinically relevant EEG signals such as epileptiform signals. This performance is necessary for the physician to monitor the indicated patient's condition using EEGs obtained with the Minder System.

The Minder System is not designed or intended to be implanted indefinitely in the patient. When the Minder System is no longer operational, this will be indicated by the 'Electrode Lead Check' in the Minder App. When this occurs, patients should discuss device replacement or removal with their physicians. The long-term safety of implanted Minder System components left in place without use, replacement, or removal is unknown.

The Minder Implant is contraindicated for all MRI and is labeled as 'MR Unsafe'. 'Magnetic Resonance (MR) Unsafe' is an item that poses unacceptable risks to the patient, medical staff, or others within an MR environment. This means that patients with the Minder Implant will not be able to undergo MRI scans without first having the device explanted. Going through MRI scans without removing the Minder Implant may result in excessive heating occurring at the location of the implanted device, or movement of the implanted magnet leading to serious patient injury or death. Please consult with the healthcare provider or Epiminder for further guidance on medical procedures while using the Minder System.

The inability for patients to undergo MRI scans without explantation of the Minder Implant may pose several long-term risks to healthcare management:

- Limited Diagnostic Capabilities: Without access to MRI scans, healthcare providers may have limited ability to accurately diagnose and monitor certain conditions.
- Delayed or Altered Treatment Plans: In cases where MRI scans are essential for treatment planning, the inability to undergo these scans may lead to delays in initiating appropriate treatment or necessitate alternative treatment

approaches that may be less effective or carry greater risks. The delayed diagnosis and treatment may potentially lead to worsened health outcomes or complications.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Minder System consists of implanted and externally worn components intended for continuously recording, transmitting, and storing EEG signals from patients between 18-75 years of age with drug-resistant epilepsy who are intolerant or not indicated for more conservative EEG monitoring tools. The externally worn Minder Wearable receives the transmitted EEG signals from the Minder Implant and wirelessly transfers the signals to a Minder App stored on a mobile phone. The patient's EEG signals can then be downloaded from the mobile phone to a server for remote viewing and analysis by a physician.

Minder Implant:
The primary functions of the Minder Implant are:

- Receive and decode control commands from the Minder Wearable.
- Record EEG signals using two distinct channels (each channel supported by 2 electrodes).
- Transfer EEG signals through the skin to the Minder Wearable using inductive link.
- Measure, record, and transfer impedances and voltages measured on each electrode to the Minder Wearable.

Figure 1: Minder Implant with telemetry unit and electrode lead.

Minder Surgical Templates:
Minder Surgical Templates are provided by Epiminder to aid the physician with implantation of the Minder Implant.

Figure 2: Minder Surgical Templates.

Minder Wearable:
The Minder Wearable is positioned behind the ear and is always worn by the user during recording. Includes ear hooks and a clip to facilitate securing the Minder Wearable to the user. Some key functions of the Minder Wearable are the following:

- Control and command the Minder Implant to acquire physiological signals and voltages.
- Store and stream real-time EEG signals and other data from the Minder Implant to the Minder App via Bluetooth Low Energy (BLE).
- Provide status information to the Minder App:
    - Coil on/off status.
    - Battery level.
    - Faults.

Figure 3: Minder Wearable components.

Smartphone:
The smartphone is a commercially available Android phone. Epiminder supplies the phone and controls the phone through a Mobile Device Manager (MDM). The phone is locked down so only the Minder App is functional. The user does not have the ability to access any other phone features or install any other apps other than the Minder App. This controls the cybersecurity and performance of the smartphone when incorporated and used in the Minder System.

Minder App:
The primary functions of the Minder App are the following:

- Collect and locally store data from the Minder Wearable via an encrypted BLE.
- Conduct Minder Implant integrity checks via electrode impedance measurements.
- Upload data to the cloud for secure storage and access.
- Record and upload patient-reported events.

Minder Cloud:
Minder Cloud is a web-based application that provides physicians secure access to patient data. The data from the cloud storage may be exported by the physician to a local computer or network drive to be viewed and analyzed using Epiminder specified EEG review software that is legally marketed for this purpose in the United States (U.S.).

The primary functions of the Minder Cloud are as follows:

- Patient administration.
- Clinic (site) and clinician registration.
- EEG and patient-reported event data export functions.
- Authentication and authorization functions for Minder App and the web-based portal, and access to data stored in Minder Cloud.
- Authenticated endpoints for Minder App to upload collected EEG data and patient-reported events.
- Ingestion, processing, storage, and export of EEG data.

- Security, privacy, logging, and auditing functionality.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY

The Minder Implant is an implanted device contacting tissue/bone for a long-term duration (> 30 days). As such, its biocompatibility evaluation was conducted in accordance with ISO 10993-1:2018, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process," and the FDA guidance, "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'." For a long-term contact implant in contact with tissue/bone, the Minder System was evaluated for the following biocompatibility endpoints: cytotoxicity, sensitization, irritation, acute systemic toxicity, material-mediated pyrogenicity, subacute/subchronic toxicity, genotoxicity, implantation, chronic toxicity and carcinogenicity. Testing for all biocompatibility endpoints were found to be adequate.

- Cytotoxicity testing in accordance with ISO 10993-5, "Biological evaluation of medical devices - Part 5: Tests for *in vitro* cytotoxicity."
- Sensitization and irritation testing in accordance with ISO 10993-10, "Biological evaluation of medical devices - Part 10: Tests for skin sensitization."
- Acute systemic toxicity testing in accordance with ISO 10993-11, "Biological evaluation of medical devices - Part 11: Tests for systemic toxicity."
- Material-mediated pyrogenicity testing in accordance with USP <151>, "Rabbit Pyrogen Study."
- Genotoxicity testing in accordance with ISO 10993-3, "Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity."
- Implantation testing in accordance with ISO 10993-6, "Biological evaluation of medical devices - Part 6: Tests for local effects after implantation."

Chemical Characterization and Toxicological Risk Assessment (TRA)
In order to assess the risks associated with the Minder Implant resulting in adverse tissue reaction or systemic toxicity effects, chemical characterization and subsequent TRA was performed on the final finished device. The TRA concluded that the extractables from the test article, Minder Implant, are unlikely to pose a toxicological safety concern. Based on the safety of the Minder Implant as assessed by chemical characterization and TRA, the systemic toxicity (subacute, subchronic, and chronic) and carcinogenicity endpoints were evaluated using this testing approach in lieu of the biological testing recommended in ISO 10993-1, annex A.

STERILITY AND SHELF-LIFE

Minder Implant

The Minder Implant and its packaging has been validated for a shelf-life of 1 year supported by performance testing using both accelerated aged and real-time aged test samples that were subjected to preconditioning and packaging distribution conditions. The results showed the final product packaging maintains product functionality and sterility under worst-case shipping, handling, and storage conditions.

The Minder Implant is provided sterile using ethylene oxide (EtO) sterilization and is intended for single use only. The final finished product is sterilized to a sterility assurance level (SAL) of 10^{-6}. Testing demonstrated that EtO residual levels resulting from the sterilization method are below the limits set in ISO 10993-7, "Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals."

Bacterial endotoxin testing using the limulus amebocyte lysate (LAL) kinetic chromogenic test method demonstrated that the Minder Implant met the endotoxin limit of ≤ 2.15 endotoxin units (EU)/device. Bacterial endotoxin testing will be performed on each lot of the Minder Implant as part of the manufacturing process.

Minder Surgical Templates
The Minder Surgical Templates are provided non-sterile and can be reused after proper reprocessing. Validated reprocessing steps for automated cleaning, thermal disinfection, and steam sterilization are included in the labeling.

ELECTROMAGNETIC COMPATIBILITY (EMC) AND ELECTRICAL SAFETY

The Minder System was tested according to the following standards:

- ANSI AAMI ES60601-1:2005/(R)2012 & A1:2012, C1:2009/(R)2012, "Medical electrical equipment - Part 1: General requirements for basic safety and essential performance."
- IEC 60601-1-2, "Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests."
- IEC 60601-1-11, "Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance - Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment."

SOFTWARE/CYBERSECURITY

Software verification and validation testing and documentation was provided according to a Basic Documentation Level per FDA's guidance document, "Content of Premarket Submissions for Software Contained in Medical Devices," published June 2023, to demonstrate that the device software performs as intended.

Cybersecurity testing and documentation was provided according to the recommendations per FDA's guidance document, "Cybersecurity in Medical

Devices: Quality System Considerations and Content of Premarket Submissions," published September 2023, to demonstrate that the device is cybersecure.

HUMAN FACTORS - USABILITY

A simulated use test was performed in which participants interacted with the device in realistic use scenarios under simulated clinical conditions. Participants were observed as they completed each task and were asked to provide subjective feedback at the conclusion of each use scenario to gain their perspectives on device use and any problems observed. Objective data was collected by observing task performance during each scenario and any problems or failure to complete a task were recorded as use errors, close calls, or use difficulties. Clinical usability testing was performed with a total of 15 healthcare professionals with experience in a neurology health care setting (e.g., can be neurologists, surgeons, registered nurses, physician assistants, nursing assistants, nurse practitioners). Patient usability testing was performed with a total of 19 participants reflective of the target patient population.

Study results indicated that participants were able to complete identified critical tasks associated with use of the device. All participants understood and were able to navigate the labeling and recite or affirm understanding of the content.

MAGNETIC RESONANCE (MR) ENVIRONMENT

Testing in an MR environment was not conducted for the Minder Implant and the device is labeled as 'MR Unsafe.'

PERFORMANCE TESTING – BENCH

Test	Purpose	Acceptance Criteria	Results
Minder Implant Impedance Measurement Capabilities	Demonstrate that the Minder Implant can measure the electrode impedances once implanted.	The implant shall be able to measure electrode impedances from 250 Ohms to 5000 Ohms with an accuracy of ±10% or 250 Ohms or whichever is greater.	Pass
Implant Electronics Operational Temperature	Demonstrate that the Minder Implant is able to meet the EEG standard/requirements when implanted (at body temperature).	The electronic assembly inside the implant shall operate within specification at 37 °C ± 2 °C for accuracy, impedance, frequency response, dynamic range, and noise.	Pass
Implant Operational Temperature	Demonstrate that the Minder Implant is able to remain operational (meet signal quality requirements) within temperatures expected in operating rooms and in vivo environments.	The implant shall remain operational between +10 °C and +43 °C.	Pass

Test	Purpose	Acceptance Criteria	Results
Lifetime of Use	Demonstrate that the Minder Implant electronics can remain operational for 10 years. This provides a factor of safety over the 3 years operational life of the implant.	The electronic assembly shall be designed and assembled to achieve an operational life of 10 years.	Pass All electronic assemblies are qualified prior to manufacturing by power burn-in testing. This testing is equivalent to 10 years accelerated age testing.
Immunity to Impact Stresses during Implantation and Handling	To verify that the Minder Implant is able to withstand environmental stresses as per ISO14708-1:2019, Clause 23.5.	Mechanical integrity of the Minder Implant body and electrode lead and electrical performance.	Pass
Immunity to Mechanical Impact Stresses during Normal Use and Trauma	To verify that the Minder Implant is able to withstand an impact at the worst-case locations on the Minder Implant body and along the electrode lead.	Minder Implant shall remain operational after withstanding 1 J impact at worst-case locations.	Pass
Immunity to Implant and In Vivo Forces.	To verify the Minder Implant, including the electrode lead, can survive implantation and accelerated life testing. Testing takes the form of high frequency cyclic tests, thermal cycling, and accelerated temperature testing.	The Minder Implant shall remain electrically and mechanically operational after simulated implant forces. The Minder Implant shall remain electrically functional after accelerated life testing.	Pass
Immunity of Implant to Explant Forces.	To verify the Minder Implant, including the electrode lead, can survive explantation forces.	The Minder Implant shall remain intact after explantation, i.e., no parts of the implant or electrode lead shall break off or dislodge during simulated explant forces.	Pass
Immunity of Implant to Atmospheric Pressure Changes	To verify that the Minder Implant can operate when subjected to operational and transportation pressure changes. Conducted per ISO 14708-1:2019, Clause 25.1.	Mechanical integrity of the hermetic seal. The Minder Implant shall remain operational.	Pass
Hermeticity	To verify the Minder Implant remains hermetically sealed in compliance with ISO 14708-7:2019, Clause 19.6.	The implant case shall provide sufficient hermeticity so that no fluid can infiltrate the implant case.	Pass
Internal Moisture Content	To show compliance to ISO 14708-7:2019 and the prescribed test limits as per ANSI/AAMI CI86:2017, "Cochlear implant systems."	The internal moisture content inside the hermetic cavity shall be less than, or equal to, 5000 ppm.	Pass

Test	Purpose	Acceptance Criteria	Results
Implant Ingress Protection	Demonstrate that the Minder Implant does not allow fluid into the non-hermetic side of the implant that may affect recording capability.	An aged implant shall not allow fluid ingress that reduces the electrode impedances below 80 kOhm.	Pass
Immunity to Diagnostic Levels of Ultrasound	ISO 14708-7, Clause 22.1 (EN45502-2-3: 2010, Clause 22.1)	The Minder System shall be designed and constructed so that no irreversible change will be caused by exposure to diagnostic levels of ultrasonic energy.	Pass
Transportation and Storage Pressure	Demonstrate that the Minder Implant can withstand pressure ranges from sea level and exposure to high altitude environmental conditions expected with air travel.	The implant shall be operational after being subjected to absolute pressures from 10 kPa to 758 kPa.	Pass
Storage and Transport Temperature	To cover transportation (e.g., high altitude, cold climates) as per ISO 14708-1:2014, Clause 26.2.	The implant shall perform normally following: - Low temperature testing in accordance with IEC 60068-2-1. - High temperature testing in accordance with IEC 60068-2-2. - Thermal cycling in accordance with IEC 60068-2-14.	Pass
Environmental Shock and Vibration	Demonstrate that the Minder Implant remains operational after being subjected to shock and vibration in compliance to ISO 14708-1:2014, Clause: 23.7, and ISO 14708-1:2014, Clause 23.2.	The implant shall remain operational after being subjected to shock and vibration to simulate transportation conditions as described in: IEC 60068-2-27:2008, IEC 60068-2-47:2005, and IEC 60068-2-64:2008.	Pass

Table 1: Performance bench testing conducted for the Minder System.

SUMMARY OF CLINICAL INFORMATION

Study Design

The clinical validation study was a prospective, open-label, case-controlled, comparator study conducted at 6 outside the United States (OUS) sites in Australia to demonstrate the safety and performance of the implantable Minder System for continuous collection of EEG recordings. The comparator used in the study was patient seizure diaries and placement of cleared scalp electrodes, in comparable quantity and location to the Minder System, in an epilepsy monitoring unit (EMU).

Inclusion Criteria

- Subject between 18 and 75 years.
- Subject speaks and reads English.
- Established clinical diagnosis of focal or generalized epilepsy as defined by the International League Against Epilepsy (ILAE) criteria.
- Subject and/or caregiver reported a minimum of two clinically identifiable epileptic events per month.
- Except for epilepsy, subject is medically and neurologically stable as defined by a clinician.
- An EEG profile consistent with diagnosis of epilepsy. Subject has had prior neuroimaging, within the past 5 years, with report available. Subjects may be enrolled by study doctors with imaging outside this interval under exceptional circumstances, provided that they are clinically stable, and the subject's underlying pathology is known to be static and non-progressive, or if the subject has a confirmed idiopathic generalized epilepsy (that are not associated with structural pathologies) where neuroimaging is not indicated.
- Subject may reasonably be expected to maintain a seizure diary and seizure monitoring device alone, or with the assistance of a competent individual.
- Subject is able to complete regular study visits and telephone appointments in accordance with the study protocol requirements.
- A female subject with a negative pregnancy test within two weeks prior to implant, and, if sexually active, using a reliable form of birth control, surgically sterile, or at least two years post-menopausal. If negative serum pregnancy test result exceeds two-week limit, then a negative result from a urine pregnancy kit within two weeks of implant required.
- Subject's anatomy permits implantation of the Minder Implant (including adequate skin flap thickness).

<u>Exclusion Criteria</u>

- Subject with significant progressive disorders or unstable medical conditions requiring acute intervention.
- Active vagus nerve stimulation (VNS), deep brain stimulation (DBS), responsive neurostimulator system (RNS) or other neurostimulation device implanted and being used for epilepsy or other conditions.
- Epilepsy surgery within 6 months prior to enrollment.
- Active suicidal plan/intent within 6 months prior to enrollment, a history of suicide attempt within 2 years prior to enrollment, or more than one lifetime suicide attempt. If time between enrollment and implant exceeds 2 months, study doctors reassess to confirm criterion is met.
- A serious psychiatric disorder including unstable depression or where changes in pharmacotherapy are needed or anticipated during the study.
- Subject ineligible for device implantation surgery including any of the following:
    - Subject taking anticoagulants and unable to discontinue them peri-surgically as required by the neurosurgeon or investigator.
    - Subject with significant platelet dysfunction from medical conditions or medications (including particularly aspirin or clopidogrel). If platelet dysfunction

suspected, subject only enrolled if hematologist, the investigator, and the neurosurgeon judge to be advisable.
    - Subject ineligible for cranial surgery.
    - Subject with an uncontrolled cardiac condition.
    - Subject with a pacemaker, implantable cardiac defibrillator or other cardiac management device implanted.
    - Subject with abnormal laboratory blood tests that the neurosurgeon or investigator feels is clinically relevant and may preclude surgery or study participation.
- Subjects who cannot consent for themselves.
- Subjects on immunosuppression medication. If immunosuppressive medication is used, subject can be enrolled only if the investigator and the neurosurgeon judge to be advisable.
- Subjects with localized scalp infection within 6 weeks prior to implantation surgery.
- Subjects anticipated to have or with a high likelihood to have the following contraindicated treatments during the study: magnetic resonance imaging (MRI), electro-convulsive therapy (ECT), lithotripsy, and diathermy.
- Subjects with international travel planned through the primary endpoint at 6-months post-implant are excluded from the study. However, emergency travel is acceptable.
- Subjects may be excluded by the study doctors based on their judgement. For example, if the subject is suspected of substance abuse or has conditions that may impact their ability to follow study procedure, their safety, or may jeopardize study participation.

Objectives

Primary Objective - Safety
To demonstrate the safety of the implantable Minder System for continuous collection of patient EEG data. Adverse events (AEs) and serious adverse events (SAEs) were collected and reported from enrollment through completion of the study period.

Secondary Objective - Effectiveness
- Comparison of seizures identified by experts reviewing the Minder System sub-scalp EEG data against subject seizure diaries (current clinical practice for counting seizures). This qualitative comparison occurred through 6-months post-implant.
- Comparison of the EEG signals collected from the Minder System against 4 scalp EEG electrodes positioned as close to the implanted Minder System sub-scalp electrodes as practically feasible. This comparison was performed by expert review of representative EEG data during activities, including but not limited to, rest, closed eyes, jaw clenching, eye blinking, eye movements, and jumping on the spot, at 4-weeks and 24-weeks post-implant.
- Comparison of seizures identified by experts during the gold standard of video and international 10-20 scalp EEG monitoring against the Minder System sub-scalp EEG at 4-weeks and 24-weeks post-implant.
- Subject acceptance and impression of usability of the device for the purpose of obtaining feedback on the system design, including coil on the head, comfort, sleeping use, battery charging, and data back-up. This information was collected using a study-specific patient questionnaire at 4-weeks and 24-weeks post-implant.

- Patient reported outcomes (PROs) evaluated at baseline, 4-weeks and 24-weeks post-implant.

Results

Enrollment

A total of 31 patients were enrolled into the study, with 26 patients being implanted with the Minder System at 6 OUS sites in Australia. Of these 26 subjects, 24 subjects were considered study completers (i.e., subjects who completed all necessary follow-up visits up to the 24-weeek period). However, data was only collected from 25 patients, due to a singular patient being ill with another condition and became unable to use the device, as indicated.

At the completion of this review, 24 subjects had entered an optional long-term follow-up period (3 years post device implantation) of the study, with 7 subjects completing the long-term follow-up period.

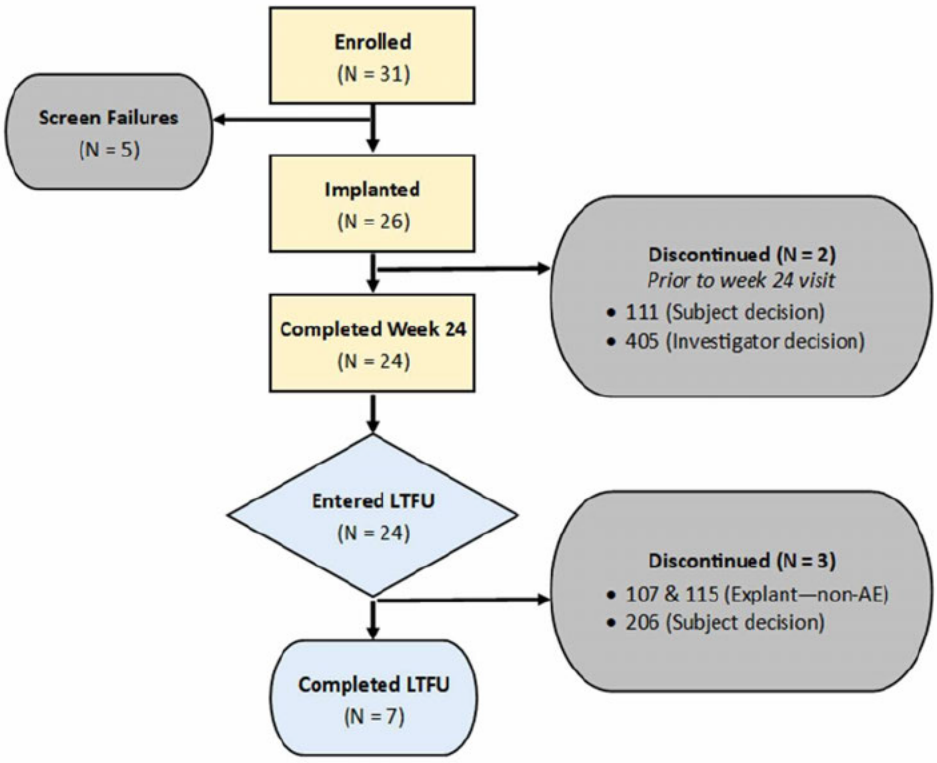

Figure 4: Study subject accountability diagram.

Table 2: Subject Demographics	
Demographic	**Total (N=26)**
Gender	
Male (%)	13 (50%)
Female (%)	13 (50%)
Age at Consent (years)	
Mean ± Std (Range)	45 ± 12.4 (23-71)

Height (cm)	
Mean ± Std (Range)	170 ± 11.6 (150-193)
Weight (kg)	
Mean ± Std (Range)	83 ± 24.4 (55-143)

Table 3: Subject Epilepsy History[1]	
Medical History	**Total (N=25[2])**
Years since diagnosis (to current)	
Mean ± Std (Range)	24 ± 16.0 (4 - 47)
Considered resistant to anti-epileptic (2 or more drugs failed)	
Yes (%)	17 (68.0%)
No (%)	8 (32.0%)*
Number of anti-epileptic drugs failed	
Mean ± Std (Range)	N=25 3.2 ± 2.1 (1 – 8)
Previously determined not to be a candidate for surgical intervention	
Yes (%)	16 (64.0%)
No (%)	9 (36.0%)

[1]Data presented in this table is from 30 September 2024.
[2]Since data was collected retrospectively, subject 405 was not able to use the Minder System due to cognitive effects of their stroke.
*4 subjects were reported as resistant with only 1 drug identified, these were considered "No."

Primary Objective – Safety

AEs observed and reported during the study were defined as mild, moderate, or severe by the following criteria:

- Mild: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- Moderate: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning.
- Severe: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

Information regarding the AE relatedness to the device and procedure, device only, procedure only, and unrelated were also gathered and reported. A total of 23 out of the 26 study subjects experienced an AE of any severity.

Table 4: Adverse Event Data (# of events)			
Relatedness	**Mild AE**	**Moderate AE**	**Severe AE**
Device and Procedure Related	3	2	0
Device Related	9	1	0
Procedure Related	13	4	0
Unrelated	50	38	7

Total = 128	**77**	44	**7**

SAEs observed and reported during the study were defined as events that:

- led to death,
- led to serious deterioration in the health of the subject, that either resulted in
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient or prolonged hospitalization, or
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigation plan, without serious deterioration in health, is not considered a serious adverse event. A total of 8 study subjects experienced a SAE.

Table 5: Serious Adverse Event Data (# of events)

Relatedness	Body System	AE Term (Coded)	Totals
Procedure-related	Infection	Wound infection	1
Unrelated	Cardiac	Sinus bradycardia	1
	Injury/Procedural	Fracture (rib)	1
		Stab wound	1
	Nervous System	Seizure(s)	11
	Psychiatric	Post-ictal psychosis	2
Totals			**17**

The majority of the AEs and SAEs observed were reported to be unrelated to the device and procedure, device itself, or procedure itself. Additionally, the most frequently observed AE was reported to be seizures, which is expected for the target patient population.

Secondary Objective - Effectiveness

- Comparison of seizures identified by experts reviewing the Minder System sub-scalp EEG data against subject seizure diaries (current clinical practice for counting seizures). This qualitative comparison occurred through 6-months post-implant. Observed results demonstrate the capability of the Minder System to provide EEG data that may be used to confirm absence or presence of specific electrographic events that may or may not be reported in patient diaries.
- Comparison of the EEG signals collected from the Minder System against 4 scalp EEG electrodes positioned as close to the implanted Minder System sub-scalp electrodes as practically feasible. This comparison was performed by expert review of representative EEG data during activities, including but not limited to, rest, closed eyes, jaw clenching, eye blinking, eye movements, and jumping on the spot, at 4-weeks and 24-weeks post-implant. Observed results support that the Minder System provides comparable EEG signal quality and noise performance to that of scalp electrodes placed in a similar

position. Observed results also confirms the stability of the EEG measurements by the Minder System between the 4-week and 24-week post-implantation period, and that clinically relevant EEG signals such as muscle artifact, sleep spindles, and interictal epileptiform events (IEEEs) were able to be identified at the 4-week and 24-week post-implantation period.

- Comparison of seizures identified by experts during the gold standard of video and international 10-20 scalp EEG monitoring against the Minder System sub-scalp EEG at 4-weeks and 24-weeks post-implant. Observed results support that the Minder System provides comparable EEG signal quality and noise performance to 10-20 scalp video EEG monitoring that can be used to identify electrographic seizure activity in patients. Observed results also confirms the stability of the EEG measurements by the Minder System between the 4-week and 24-week post-implantation period with sufficient signal noise and quality to identify electrographic seizure activity in patients.
- Subject acceptance and impression of usability of the device for the purpose of obtaining feedback on the system design, including coil on the head, comfort, sleeping use, battery charging, and data back-up. This information was collected using a study-specific patient questionnaire at 4-weeks and 24-weeks post-implant. It was observed that most of the study patients were compliant with the use and wear of the Minder System. Non-compliant patients were due to cosmetic reasons, external components causing pain or discomfort, extra thick skin flap causing attachment issues with the external components, or other illness affecting use of the device.
- PROs evaluated at baseline, 4-weeks, and 24-weeks post-implant. Results from Quality of Life in Epilepsy (QOLIE-89), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Liverpool Seizure Severity Scale (LSSS) v2.0 scores at baseline versus week 4 and baseline versus week 24 did not show a significant difference in scores.

Pediatric Extrapolation

In this De Novo request, existing clinical data from the study for patients ages 23-71 was extrapolated to demonstrate safety and effectiveness in transitional adolescent pediatric patients 18 to < 22 years old but treated as adults. No differences are expected between adults and transitional adolescents 18 to < 22 years old.

LABELING

The labeling is sufficient and satisfies the requirements of 21 CFR 801.109 for prescription devices.

The labeling includes a detailed description of the device system, a summary of the in vivo performance testing conducted to demonstrate device safety and performance under anticipated use conditions, the device technical parameters, explanation of all device outputs, care instructions to maintain the operation of the device, operational life and duration of device implantation, instructions for the surgical procedure and explantation of the Minder Implant, and troubleshooting options. The patient labeling includes a discussion of what to expect regarding the surgical procedure, accompanied by a discussion of alternatives available to the patient, if applicable. The labeling warns that the device is “MR Unsafe”, which limits the ability of

patients implanted with the Minder System to receive MRI scans to diagnose or monitor certain conditions. The labeling warns and cautions against any medical environments or use with other devices that may not be compatible with the Minder System and could raise safety risks to the patients or damage or interfere with the accuracy, reliability, or functionality of the device measurement and operation. The labeling also indicates that the device is not a standalone diagnostic, and the device output must be reviewed and interpreted by a qualified healthcare professional. The labeling indicates that the device does not provide any diagnostic conclusions about the patient's condition.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a sub-scalp implanted electroencephalogram system for remote patient monitoring and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Inaccurate EEG measurement leading to: • Delayed diagnosis and/or patient treatment • Inappropriate or incorrect patient treatment	In vivo performance testing Software verification, validation, and hazard analysis Non-clinical performance testing Electromagnetic compatibility testing Labeling
Tissue injury resulting from • Device breakage • Use error	In vivo performance testing Labeling
Infection	Sterilization validation Reprocessing validation Shelf-life testing Labeling
Device malfunction leading to injury to user/patient (e.g., shock, burn, interference)	In vivo performance testing Non-clinical performance testing Electrical, mechanical, and thermal safety testing Software verification, validation, and hazard analysis Electromagnetic compatibility testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the sub-scalp implanted electroencephalogram system for remote patient monitoring is subject to the following special controls:

(1) In vivo performance testing must demonstrate that the device performs as intended following implantation to continuously acquire, transmit, and store electrical brain activity and evaluate all adverse effects, including tissue injury.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use for the duration of the operational life of the device. The technical specifications of the device's hardware and software must be fully characterized, such as:
    (i) Data acquisition testing:
        (A) Input dynamic range;
        (B) Signal/noise ratio;
        (C) Frequency response;
        (D) Accuracy and resolution of recorded signal; and
        (E) Quality and accessibility of continuous wireless transmission.
    (ii) Mechanical testing:
        (A) Impact testing; and
        (B) Integrity testing following implantation and explantation.

(3) Performance testing must evaluate the compatibility of the device in a magnetic resonance environment.

(4) The patient-contacting components of the device must be demonstrated to be biocompatible.

(5) Performance testing must demonstrate electrical safety, thermal safety, mechanical safety, electromagnetic compatibility (EMC), and wireless coexistence of the device in the intended use environment.

(6) Software verification, validation, and hazard analysis must be performed.

(7) Performance testing must demonstrate the sterility of the device.

(8) Performance data must support the shelf-life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf-life.

(9) Performance testing must validate the reprocessing instructions for the reusable components of the device.

(10) Physician and patient labeling must include the following:
    (i) Detailed description of the device technical parameters, explanation of all device outputs, care instructions to maintain the operation of the device, operational life and duration of device implantation, and troubleshooting options;
    (ii) A summary of any in vivo performance testing conducted to demonstrate device safety and performance under anticipated use conditions;
    (iii) Conditions of use that may impact the accuracy, reliability, or functionality of the device measurement and operation;
    (iv) Conditions that may preclude use and implantation of the device, such as skin integrity or thickness;
    (v) Magnetic resonance imaging related information;
    (vi) Statement that the device is not a standalone diagnostic device and does not replace clinical decision making; and

(vii) A shelf-life.

(11) Physician labeling must include:
   (i) Instructions for the preparation and implantation of the device, including recommended site of implantation and method of implantation, and explantation of the device; and
   (ii) Validated instructions for reprocessing of any reusable component.

(12) Patient labeling must include:
   (i) A patient implant card, including magnetic resonance imaging related information;
   (ii) Information about the associated surgical procedure; and
   (iii) A discussion of available monitoring alternatives.

BENEFIT-RISK DETERMINATION

The risks of the device are based on data collected in the clinical study described above, in addition to non-clinical performance testing, biocompatibility evaluations, sterilization validation, EMC testing, electrical safety, thermal safety, mechanical safety testing, and hardware and software verification, validation, and hazard analysis.

The clinical study observed 128 AEs and 17 SAEs that were reported in 23 patients. Thirty-two (32) of 128 AEs reported were classified to be device, procedure, or device and procedure related where most were considered mild or moderate in severity. The most common AE reported was for pain near the implant site or headache. One (1) of 17 SAEs reported was classified to be procedure related. One patient reported infection at the location of the Minder Implant. The infection occurred at the patient's 4-week follow-up and is believed to have been caused by excessive rubbing of the scalp when prepping the patient for the application of scalp electrodes. The infection was treated with antibiotics and the patient fully recovered within 30 days and the patient did not require hospitalization or removal of the device.

The Minder System is labeled as 'MR Unsafe.' It is possible that the targeted patient population may need to undergo magnetic resonance (MR) imaging and having the Minder System implanted will preclude patients from being scanned, which may limit diagnostic capabilities of neuroimaging or delay or alter treatment plans. Patients will need to undergo device explantation prior to being scanned.

The probable benefits of the device are based on the data collected in the clinical study described above, in addition to non-clinical performance testing and hardware and software verification, validation, and hazard analysis.

The prospective, open-label, case-controlled, comparator study of 26 implanted patients, conducted at 6 OUS sites in Australia, demonstrated that the Minder System provides stable long-term EEG recording that is comparable in signal quality and noise performance to that of scalp electrodes placed in a similar position. The Minder System can monitor EEG for epilepsy patients outside of clinical care settings that is not currently available. This is expected to provide

more reliable data that can be used with a clinician's assessment in comparison to, but in conjunction with, existing methods such as patient diaries.

Additional benefit/risk factors include patient tolerance for risk and risk mitigations due to the device's design. Patients are likely to tolerate uncertainty in benefit because the device offers long-term, continuous EEG data that is currently not available for the drug-resistant epilepsy population. This is evident in that, as a designated Breakthrough Device, no other cleared or approved devices address the medical need being met by the Minder System. Although there are other clinical options that address this medical need, this device offers a long-term objective monitoring option that can be used in the home setting.

For the reasons described above, the probable benefits of the Minder System outweigh the probable risks when considering the listed special controls and the general controls.

PATIENT PERSPECTIVES

As part of the clinical study, subjects were provided with a number of PROs that were used to determine monitoring changes with the Minder System. These patient questionnaires included the Quality of Life in Epilepsy (QOLIE-89), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Liverpool Seizure Severity Scale (LSSS) v2.0. The Minder System is not intended to be a therapy; therefore, it was expected that there would be no significant changes in the PROs, and this was confirmed during the study. At the baseline versus 4-week and baseline versus 24-week comparisons in these PROs, it was observed that there were no statistically significant differences in scores and there does not appear to be any negative changes to patients due to the introduction of the Minder System.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> "The Minder System is an electroencephalographic (EEG) recording and transmitting device implanted under the scalp. It is a prescription device indicated to acquire, transmit, and store EEGs continuously from patients between 18-75 years of age with drug-resistant epilepsy who are intolerant or not indicated for more conservative monitoring tools. The Minder System is intended to aid in a physician's remote assessment and monitoring of the indicated patient's condition. Remote patient assessment and monitoring for this use is defined as the patient's EEG data is available for review by a healthcare provider located at a different location from the patient and where the data is being collected.
>
> The medical use of the data acquired by the Minder System is to be performed under the direction and interpretation of a licensed medical professional. The Minder System does not provide any diagnostic conclusions about the patient's condition."

The probable benefits outweigh the probable risks for the Minder System. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo for the Minder System is granted and the device is classified as follows:

Product Code: SEM
Device Type: Sub-scalp implanted electroencephalogram system for remote patient monitoring
Regulation Number: 21 CFR 882.1360
Class: Class II