May 23, 2023

Ceribell, Inc.
Raymond Woo, Ph.D.
Chief Technology Officer
360 N Pastoria Ave.
Sunnyvale, CA 94085

Re: K223504
Trade/Device Name: Ceribell Status Epilepticus Monitor
Regulation Number: 21 CFR 882.1400
Regulation Name: Electroencephalograph
Regulatory Class: Class II
Product Code: OMB
Dated: April 28, 2023
Received: April 28, 2023

Dear Raymond Woo:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Patrick Antkowiak -S

Patrick Antkowiak, Ph.D.
Acting Assistant Director
DHT5A: Division of Neurosurgical,
Neurointerventional
and Neurodiagnostic Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K223504

Device Name
Ceribell Status Epilepticus Monitor

Indications for Use *(Describe)*
The Ceribell Status Epilepticus Monitor software is indicated for the diagnosis of Electrographic Status Epilepticus in patients greater than or equal to 18 years of age who are at risk for seizure. The Ceribell Status Epilepticus Monitor software analyzes EEG waveforms and identifies patterns that may be consistent with electrographic status epilepticus as defined in the American Clinical Neurophysiology Society's Guideline 14.

The diagnostic output of the Ceribell Status Epilepticus Monitor is intended to be used as an aid for determining patient treatment in acute-care environments. The device's diagnosis of Electrographic Status Epilepticus provides one input to the clinician that is intended to be used in conjunction with other elements of clinical practice to determine the appropriate treatment course for the patient.

The Ceribell Status Epilepticus Monitor is intended for diagnosis of Electrographic Status Epilepticus only. The device does not substitute for the review of the underlying EEG by a qualified clinician with respect to any other types of pathological EEG patterns. The device is not intended for use in Epilepsy Monitoring Units.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This summary of 510(k)-safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Applicant Information:

Ceribell, Inc.
360 N Pastoria Ave
Sunnyvale, CA 94085

Contact Person:

Raymond Woo, Ph.D.
CTO
Telephone: (650) 556-4349
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Subject Device Information:

Trade Name:	Ceribell Status Epilepticus Monitor
Classification Name:	Electroencephalograph
Device Class:	II; 21 CFR 882.1400
Product Code:	OMB
OMB Device:	Automatic Event Detection Software for Full-Montage Electroencephalograph

Predicate Device:

K191301
Ceribell Pocket EEG Device
882.1400, OMB (automatic event detection software for full-montage electroencephalograph), OMC, GWQ

Date Prepared:

May 18, 2023

Device Description:

The Ceribell Status Epilepticus Monitor is a software as medical device that analyzes EEG waveforms for the intended use of recognizing electrographic status epilepticus (ESE). The subject device software is intended for use only with the Ceribell Pocket EEG Device (K191301), which is also the predicate device. The predicate device contains a software module that performs detection of seizures in a similar manner as the subject device. The user workflow and instructions for starting an EEG recording on a patient are unchanged compared to the predicate device.

The user places the Ceribell Instant EEG Headband (K210805) on the patient, the headband contains 10 electrodes that are arranged in a bipolar montage and correspond to the following locations following the

10-20 electrode naming convention: Fp1, F7, T3, T5, O1, Fp2, F8, T3, T6, O2. The 10 electrodes form 8 channels (4 on the left hemisphere, 4 on the right hemisphere) that are analyzed by the subject device's ESE detection algorithm. The American Clinical Neurophysiology Society's (ACNS) Guideline 14 ("Standardized Critical Care EEG Terminology: 2021 Edition") defines ESE as follows:

> ESE is defined as an ESz [electrographic seizure] for ≥ 10 continuous minutes or for a total duration of ≥ 20% of any 60-minute period of recording.

By definition, ESE is a finding that is based solely on the characteristics of the subject's EEG waveforms. The are no other clinical considerations or sources of clinical information that are used in the determination of ESE. The subject device is intended for use in the recognition of ESE in acute care environments only. The absence of a detection of ESE by the subject device does not preclude the possibility that seizures, other epileptiform patterns, or other pathologies are present in the EEG recording. The device does not substitute for the review of the underlying EEG by a qualified clinician with respect to any other types of pathological EEG patterns.

Intended Use

The Ceribell Status Epilepticus Monitor is a software as medical device that is intended to analyze EEG recordings captured with the Ceribell Pocket EEG Device and the Ceribell Instant EEG Headband and diagnose electrographic status epilepticus in patients greater than or equal to 18 years of age who are at risk for seizure. The software analyzes EEG waveforms and identifies patterns that may be consistent with electrographic status epilepticus as defined in the American Clinical Neurophysiology Society's Guideline 14.

The diagnostic output of the Ceribell Status Epilepticus Monitor is intended to be used as an aid for determining patient treatment in acute-care environments. The device's diagnosis of Electrographic Status Epilepticus provides one input to the clinician that is intended to be used in conjunction with other elements of clinical practice to determine the appropriate treatment course for the patient.

The Ceribell Status Epilepticus Monitor is intended for diagnosis of Electrographic Status Epilepticus only. The device does not substitute for the review of the underlying EEG by a qualified clinician with respect to any other types of pathological EEG patterns. The device is not intended for use in Epilepsy Monitoring Units.

Comparison of Intended Use and Technological Characteristics with the Predicate Device:

The subject device is substantially equivalent to the seizure detection module of the predicate device in terms of intended use, operating principles, and design. The subject device and predicate devices both contain algorithms to detect electrographic seizures, and in both the subject device and predicate device the design of the electrographic seizure detection is the same. Then the subject device additionally processes the electrographic seizure detections to make a determination regarding ESE. The ESE determination serves as the final output of the subject device. The device output is binary: ESE is either detected or not detected.

Table 1. Comparison between the subject device and predicate device.

Attribute	**Subject Device** Ceribell Status Epilepticus Monitor	**Predicate Device** Ceribell Pocket EEG Device (K191301)
Intended Use	The Ceribell Status Epilepticus Monitor is a software as medical device that is intended to analyze EEG recordings captured with the Ceribell Pocket EEG Device and the Ceribell Instant EEG Headband and diagnose electrographic status epilepticus in patients greater than or equal to 18 years of age who are at risk for seizure. The software analyzes EEG waveforms and identifies patterns that may be consistent with electrographic status epilepticus as defined in the American Clinical Neurophysiology Society's Guideline 14. The diagnostic output of the Ceribell Status Epilepticus Monitor is intended to be used as an aid for determining patient treatment in acute-care environments. The device's diagnosis of Electrographic Status Epilepticus provides one input to the clinician that is intended to be used in conjunction with other elements of clinical practice to determine the appropriate treatment course for the patient. The Ceribell Status Epilepticus Monitor is intended for diagnosis of Electrographic Status Epilepticus only. The device does not substitute for the review of the underlying EEG by a qualified clinician with respect to any other types of pathological EEG patterns. The device is not intended for use in Epilepsy Monitoring Units.	The Ceribell Pocket EEG Device is a portable EEG monitoring system that records, stores and presents EEG signals in visual and audible formats in real time. The visual and audible signals assist trained medical staff to make neurological diagnoses. The Pocket EEG Device EEG Recording Viewer software incorporates a seizure detection component is intended to analyze EEG recordings captured with the Ceribell Pocket EEG Device and identify areas that may correspond to electrographic seizures in patients greater or equal to 18 years of age. The Pocket EEG Device seizure detection module is not intended to provide clinical conclusions about the subject's condition and the output of the seizure detection module is intended to be used by qualified clinical practitioners in coordination with other clinical observations.
Indications for Use	The Ceribell Status Epilepticus Monitor software is indicated for the diagnosis of Electrographic Status Epilepticus in patients greater than or equal to 18 years of age who are at risk for seizure. The Ceribell Status Epilepticus Monitor software analyzes EEG waveforms and identifies patterns that may be consistent with electrographic status epilepticus as defined in the American Clinical Neurophysiology Society's Guideline 14. The diagnostic output of the Ceribell Status Epilepticus Monitor is intended to be used as an aid for determining patient treatment in acute-care environments. The device's diagnosis of Electrographic Status Epilepticus provides one input to the clinician that is intended to be used in conjunction with other elements of clinical practice to determine the appropriate treatment course for the patient. The Ceribell Status Epilepticus Monitor is intended for diagnosis of Electrographic Status Epilepticus only. The device does not substitute for the review of the underlying EEG by a qualified clinician with respect to any other types of pathological EEG patterns. The device is not intended for use in Epilepsy Monitoring Units.	The Ceribell Pocket EEG Device is intended to record and store EEG signals, and to present the EEG signals in visual and audible formats in real time. The visual and audible signals assist trained medical staff to make neurological diagnoses. The Pocket EEG Device is intended to be used in a professional healthcare facility environment. Additionally, the EEG Recording Viewer Software component of the Pocket EEG Device incorporates a Seizure Detection component that is intended to mark previously acquired sections of EEG recordings in patients greater than or equal to 18 years of age that may correspond to electrographic seizures in order to assist qualified clinical practitioners in the assessment of EEG traces. The Seizure Detection component provides notifications to the user when detected seizure prevalence is "Frequent," "Abundant," or "Continuous," per the definitions of the American Clinical Neurophysiology Society Guideline 14. Notifications include an on-screen display on the Pocket EEG Device and the optional sending of an e-mail message to a clinician. Delays of up to several minutes can occur between the beginning of a seizure and when the Seizure Detection notifications will be shown to a user. The Pocket EEG Device does not provide any diagnostic conclusion about the subject's condition and Seizure Detection notifications cannot be used as a substitute for real time monitoring of the underlying EEG by a trained expert.
Intended User	Qualified healthcare professional	Qualified healthcare professional

Attribute	Subject Device Ceribell Status Epilepticus Monitor	Predicate Device Ceribell Pocket EEG Device (K191301)
Intended Patient population	Patients greater or equal to 18 years of age.	All ages. The seizure detection module is intended only for patients greater or equal to 18 years of age.
Intended Location of Use	Acute-care environments within professional healthcare facilities	Professional healthcare facility

Performance Data:

Bench-top verification testing was performed on the subject device. The verification tests were completed in accordance with relevant standards and pre-approved protocols to evaluate the safety and performance of the subject device, and all tests were passed.

Table 2. Summary of bench-top verification testing.

Test Description	Acceptance Criteria	Test Results
ESE Monitor System Level Test: Integration and system level test that verifies and validates the processing of ESE data and the display of ESE output (ESE detected/ESE not detected).	Various functional acceptance criteria based on the expected behavior of the system.	All tests passed.
Regression Testing: Per the V&V Summary Report, several test protocols were executed to ensure that the Status Epilepticus Monitor did not have any unexpected effect or cause unintended regressions with the underlying Pocket EEG Device software. Because these test reports do not directly verify any of the subject device software requirements, all of these regression test reports are combined into a single appendix for simplicity.	Various functional acceptance criteria based on the expected behavior of the system.	All tests passed.

Clinical Testing

A retrospective clinical validation study was performed by analyzing the subject device algorithm's performance using previously-collected EEG data. The objective of the study design was to obtain a dataset that is representative of the intended patient population, and this was accomplished by using real-world data. The methodology of data collection was as follows:

- For each of 6 hospitals of varying size and geographic location:
  - Collect all clinically performed Ceribell EEGs from a fixed one-year time period
  - Exclude any EEGs from patients < 18 years of age
  - There were no other inclusion or exclusion criteria applied

- Categorize each subject as ESE-positive or ESE-negative by having a team of qualified neurologists independently review and categorize each EEG; the ground-truth reference standard is established by a majority opinion of the expert reviewers

This data collection method resulted in a dataset of 350 subjects representative of the intended patient population. The demographic distribution of the subjects is shown in the following tables.

Table 3. Validation dataset age demographics showing included and excluded subjects.

Subject Age (years)	Included Subjects	Excluded Subjects	Percent of Total Included Subjects
< 18	0	3	N/A
18-20	4	0	1%
21-30	14	0	4%
31-40	23	0	7%
41-50	40	0	11%
51-60	39	0	11%
61-70	79	0	23%
71-80	63	0	18%
81-90	73	0	21%
>90	15	0	4%
Total:	350	3	
Mean Age of Included Subjects:	65.3		

Table 4. Distribution of patient gender in the validation dataset.

Subject Gender	N	Percent of Total
Male	188	54%
Female	162	46%
Total:	350	

The expert neurologist review of the EEGs resulted in a reference-standard dataset that included 10 ESE-positive subjects out of the 350 total subjects. The ESE-negative cases were further subdivided into ESE-negative cases that contained seizure and/or other epileptiform activity versus ESE-negative cases that do not contain any epileptiform activity. This categorization of the ESE-negative cases is only for data analysis and benefit-risk analysis purposes. The output of the subject device is only ESE-positive or ESE-negative.

Table 5. Expert neurologist reference standard categorization of the validation dataset.

Ground-Truth Classification	N
ESE-positive	10
ESE-negative: contains seizures and/or other epileptiform activity	94
ESE-negative: does not contain any epileptiform activity	246
Total:	350

After the clinical validation dataset was compiled, the subject device algorithm was run on the dataset and the results compared to the reference-standard. The resulting sensitivity was 100% and the specificity was 94%. There were 10 true-positive detections and 0 false-negative detections (100% sensitivity). There were 319 true-negative detections and 21 false-positive detections (94% specificity). Of the 21 false-positive detections, 19 were determined by the expert reviewers to contain seizures or other epileptiform activity.

Because the algorithm performed with 100% sensitivity in a small sample size of 10 ESE true-positive detections, there are limitations to the utility of calculating 95% confidence interval using the BCa Bootstrap method (as was done with the predicate device). As a result, two additional confidence interval calculation methods were also applied: the Wilson interval and the Jeffreys interval.

Table 6. Sensitivity and specificity results of the clinical performance validation along with the 95% confidence interval computed with three different methodologies.

	Result	95% Confidence Interval BCa Bootstrap	95% Confidence Interval Wilson	95% Confidence Interval Jeffreys
Sensitivity	100%	[100%, 100%]	[72%, 100%]	[78%, 100%]
Specificity	94%	[91%, 96%]	[91%, 96%]	[91%, 96%]

Benefit Risk Analysis

Analysis of the benefits and risks of the subject device is performed according to the FDA guidance document "Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics." (September 2018). Ceribell believes that the submitted performance validation data clearly demonstrates significant benefit of the subject device due to the magnitude and the probability of the benefit of faster diagnosis of ESE. At the same time, the identified risks of the subject device are of low probability and low severity, post-mitigation.

The greatest benefits of the subject device are specifically tied to the intended use of diagnosing electrographic status epilepticus. The maximum benefit of the subject device occurs when ESE is recognized and diagnosed during the time prior to the availability of a qualified neurologist to perform a

full review of the underlying EEG. Initiation of treatment for Status Epilepticus is highly time sensitive, yet in the standard-of-care workflow it can take 12-24 hours just to get the EEG read by a qualified neurologist. The diagnosis of ESE provided by the subject device allows administration of first-line anti-seizure medications (ASMs) and initiation of other time-sensitive actions to be performed as quickly and as accurately as possible by the intensivist and other members of the bedside critical care team. At the same time, the subject device does not replace the full review of the underlying EEG by a qualified neurologist because pathologies other than ESE may be present in the EEG.

Risks of the subject device can be categorized into risks associated with false-positive detections, false-negative detections, device malfunctions, or device misuse. In general, these risks are all low in part due to the fact that in all potential cases of failure of the subject device, the patient remains no worse off compared to the current standard-of-care, where the intensive care physician is forced to make a treatment decision without having EEG data available.

Table 7 and Table 8 on the following pages provide a detailed analysis of the benefits and risks of the subject device.

Conclusion:

The performance demonstrated in the clinical validation study clearly demonstrate that the benefits of the subject device outweigh the risks.

The Ceribell Status Epilepticus Monitor has the same intended use as the predicate devices. In addition, it has similar technological characteristics and performance data demonstrates that any differences in technological characteristics do not raise different questions of safety or effectiveness. Therefore, the Ceribell Status Epilepticus Monitor is substantially equivalent to the cleared predicate device.

Table 7. Benefits analysis of the subject device.

Benefits	Magnitude of Benefit	Probability of Benefit	Overall Benefit Evaluation
Patient with ESE is treated with ASMs 12-24 hours faster compared to the current standard-of-care when the subject device correctly identifies that ESE is present.	**High** As discussed above, early identification and treatment of ESE is associated with significantly lower morbidity and mortality.	**High** The subject device was 100% sensitive to ESE in the performance validation study.	**High**
Patient without ESE avoids unnecessary treatment with ASMs when the subject device correctly determines that ESE is not present.	**Low** Ruling out ESE may avoid unnecessary patient treatment. However, this benefit is "low" because the use of ASMs in hospital environments is commonplace and carries relatively low risk because of the clinicians' familiarity with management of these medications.	**High** The performance validation study showed that the subject device had 94% specificity.	**Low**

Table 8. Risks analysis of the subject device.

Risk	Severity	Mitigations	Risk Probability (post-mitigation)	Overall Risk Evaluation
False-positive: Subject device diagnoses ESE when ESE is not present. Patient is treated with ASMs even though they are not in status epilepticus	**Moderate** The use of ASMs in controlled hospital environments (with or without confirmation of seizures through EEG) is commonplace and carries relatively low risk because of the clinicians' familiarity with management of these medications. As with any sedative medication, there is risk of over-sedation.	• The subject device is designed such that the majority of "false-positive" cases still contain seizures or other abnormal epileptiform patterns. In these cases, treatment with ASMs may still be beneficial to the patient. • Full review of the EEG by a qualified neurologist (potentially 12-24 hours later) may determine that ASM treatment can be discontinued.	**Low** The performance validation study results showed there were 21 "false positives" out of 350 cases (6%) and 19 of the 21 "false-positive" cases (90.5%) still contained seizures or other epileptiform patterns where treatment with ASMs may still have been beneficial.	**Low**
False-negative: Subject device fails to diagnose ESE when ESE is present Treatment with ASMs is delayed.	**High** Delayed treatment of status epilepticus results in worse outcomes. <u>However, this scenario is equivalent to the current standard-of-care.</u>	• The subject device is designed to be highly sensitive to minimize the risk of "false-negative" cases. • The intensivist may still elect to treat the patient with ASMs based on other clinical observations; the EEG will still be reviewed by a qualified neurologist – the patient is no worse off than they would have been in the current standard-of care without the subject device.	**Low** The performance validation study showed that the subject device was 100% sensitive to ESE.	**Low**

Risk	Severity	Mitigations	Risk Probability (post-mitigation)	Overall Risk Evaluation
Device malfunction: Subject device fails to provide output.	**Low** The user can revert to the current standard-of-care practice	• The subject device alerts the user if the ESE detected/not-detected output is not available. The user can revert to the current standard-of-care without the subject device output.	**Low** Verification and validation testing confirm that the subject device meets its design requirements.	**Low**
Device misuse: User incorrectly utilizes the output of the subject device (i.e., uses the device output to make clinical determinations outside of the diagnosis of ESE).	**Moderate** Depending on the patient's condition, this may involve over-treatment or delayed-treatment with ASMs.	• The subject device is only capable of providing a binary diagnostic output of ESE detected/ESE not-detected. A qualified neurologist must review the EEG for other possible abnormal epileptiform findings – this limits the potential for device misuse. • The use of ASMs in controlled hospital environments (with or without confirmation of seizures through EEG) is commonplace and carries relatively low risk because of the clinicians' familiarity with management of these medications. As with any sedative medication, there is risk of over-sedation.	**Low**	**Low**