



March 8, 2024

Beacon Biosignals, Inc.
Delphine Lemoine
Senior Regulatory Affairs Specialist
22 Boston Wharf Road
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Boston, Massachusetts 02210

Re: K233438
Trade/Device Name: SleepStageML
Regulation Number: 21 CFR 882.1400
Regulation Name: Electroencephalograph
Regulatory Class: Class II
Product Code: OLZ
Dated: February 9, 2024
Received: February 9, 2024

Dear Delphine Lemoine:

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 (the 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 available 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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an

established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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

for
Jay Gupta
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

Indications for Use

Submission Number (if known)

K233438

Device Name

SleepStageML

Indications for Use (Describe)

SleepStageML is intended for assisting the diagnostic evaluation by a qualified clinician to assess sleep quality from level 1 polysomnography (PSG) recordings in a clinical environment in patients aged 18 and older.

SleepStageML is a software-only medical device to be used to analyze physiological signals and automatically score sleep stages. All outputs are subject to review by a qualified clinician.

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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Submitter

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Date Submitted: October 13, 2023

Subject Device

Trade Name: SleepStageML

Common Name: SleepStageML

Product Code: OLZ

Regulatory Class: II (21 C.F.R. 882.1400)

Review Panel: Neurology

Predicate Device: Sleep Profiler (K153412, Advanced Brain Monitoring, Inc.)

Reference Device: SomnoMetry (K221179, Neumetry Medical Inc.)

Device description

SleepStageML is an Artificial Intelligence/Machine Learning (AI/ML)-enabled software-only medical device that analyzes polysomnography (PSG) recordings and automatically scores sleep stages. It is intended for assisting the diagnostic evaluation by a qualified clinician to assess sleep quality in patients aged 18 and older.

Qualified clinicians (also referred to as clinical users) such as sleep physicians, sleep technicians, or registered PSG technologists (RPSGTs) who are qualified to review PSG studies, provide PSG recordings in European Data Format (EDF) file format through a secure file transfer system to Beacon Biosignals. SleepStageML automatically analyzes the provided PSG recording and return an EDF file containing the original PSG recording with software-generated sleep stage annotations (i.e., Wake (W), non-REM 1 (N1), non-REM 2 (N2), non-REM 3 (N3), and REM (R)) back to the clinical user. The EDF files containing PSG signals as well as sleep stage annotations are referred to as EDF+. The returned EDF+ files can then be reviewed by the qualified clinicians via the users' PSG viewing software. The recordings processed by SleepStageML are level-1 PSG recordings obtained in an attended setting in accordance with American Association of Sleep Medicine (AASM) recommendations with respect to minimum sampling rate, electroencephalography (EEG) channels, and EEG locations. SleepStageML only uses the EEG signals in provided PSGs and does not consider electromyography (EMG) or electrooculography (EOG) signals when performing sleep staging. The sleep stage outputs of SleepStageML are intended to be comparable to sleep stages as defined by AASM guidelines. SleepStageML software outputs are subject to qualified clinician's review.

The intended patients for PSG studies include those who are suspected of having, or have been diagnosed with, a sleep or sleep-related disorder. This could include sleep disordered breathing, insomnia, periodic limb movement disorder, narcolepsy, hypersomnia, or other parasomnias.

SleepStageML uses a deep learning algorithm based on convolutional neural networks, which was trained on a large and diverse set of PSG recordings with sleep staging labels.

The recordings used for development were collected from a variety of sources containing a wide range of patient demographics and clinical sites for robust performance.

Indication for Use

SleepStageML is intended for assisting the diagnostic evaluation by a qualified clinician to assess sleep quality from level 1 polysomnography (PSG) recordings in a clinical environment in patients aged 18 and older.

SleepStageML is a software-only medical device to be used to analyze physiological signals and automatically score sleep stages. All outputs are subject to review by a qualified clinician.

Indication for Use Comparison and Technological Characteristics Comparison

SleepStageML uses an automated algorithm that performs signal preprocessing and categorizes each epoch as one of the defined sleep stages using a machine learning classifier. It has similar intended use and indications for use as the predicate device Sleep Profiler (K153412, Advanced Brain Monitoring, Inc.). The predicate device does not explicitly mention the use of AI/ML, therefore, SomnoMetry (K221179, Neumetry Medical Inc.), which does use a similar AI/ML-based algorithm for staging sleep, was added as the reference device. Verification and validation methods utilized to evaluate safety and efficacy of SleepStageML were consistent with methods used for evaluating the predicate and reference devices. Software documentation was provided as recommended in FDA “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices” dated June 14th, 2023, and the pivotal clinical validation study confirmed that the SleepStageML AI/ML software performance was substantially equivalent to that of the predicate device.

Element	Subject device SleepStageML	Predicate Device Sleep Profiler (K153412)	Reference Device SomnoMetry (K221179)	Comparison of Technological Characteristics
Classification	Class II, OLZ, Automated Event Detection Software for Polysomnograph with Electroencephalograph	Class II, OLZ, Automated Event Detection Software for Polysomnograph with Electroencephalograph	Class II, OLZ, Automated Event Detection Software for Polysomnograph with Electroencephalograph	Same.
Indication for use	SleepStageML is intended for assisting the diagnostic evaluation by a qualified clinician to assess sleep quality from level 1 polysomnography (PSG) recordings in a clinical environment in patients aged 18 and older. SleepStageML is a software-only medical device to be used to analyze physiological signals and automatically score sleep stages. All outputs are subject to review by a qualified clinician.	Sleep Profiler is intended for use for the diagnostic evaluation by a physician to assess sleep quality and score sleep disordered breathing events in adults only. The Sleep Profiler is a software-only device to be used under the supervision of a clinician to analyze physiological signals and automatically score sleep study results; including the staging of sleep, detection of arousals, snoring and sleep disordered breathing	SomnoMetry is intended for use for the diagnostic evaluation by a physician to assess sleep quality and as an aid for the diagnosis of sleep and respiratory-related sleep disorders in adults only. SomnoMetry is a software-only medical device to be used to analyze physiological signals and automatically score sleep study results, including the staging of sleep, AHI, and detection of sleep-disordered breathing	Similar. SleepStageML only assists a qualified clinician in assessing sleep staging and does not include outputs related to sleep disordered breathing.

		events (obstructive apneas, hypopneas and respiratory event related arousals). Central and mixed apneas can be manually marked within the records	events including obstructive apneas. It is intended to be used under the supervision of a clinician in a clinical environment. All automatically scored events are subject to verification by a qualified clinician.	
Patient population	Adults only (≥ 18 years old)	Adults only	Adults only	Similar. SleepStageML is cleared for individuals 18 years and older, while the predicate and reference devices are cleared for individuals adults 22 years and older.
Sleep staging guidelines	American Academy of Sleep Medicine scoring manual and guidelines.	American Academy of Sleep Medicine scoring manual and guidelines.	American Academy of Sleep Medicine scoring manual and guidelines.	Same.
Environment of use	Professional Healthcare Facility	Professional Healthcare Facility	Professional Healthcare Facility	Same.
Score sleep staging	Yes	Yes	Yes	Same.
Algorithm description	Automated algorithm that performs signal preprocessing and categorizes each epoch as one of the defined sleep stages using a machine learning classifier.	Automated algorithm which spectrally decomposes the EEG signal, computes descriptors of sleep macro- and microstructure, and categorizes each epoch as one of the defined sleep stages	A broad array of signal processing, data indexing, conventional machine learning and deep learning algorithms/approaches are applied to the raw signals to derive actionable clinical insights.	Same. SleepStageML utilizes machine learning and deep learning in a similar fashion as predicate and reference devices.
Physical Characteristics	User requires a computer with access to the internet to provide original PSG recordings in EDF files to and receive returned EDF+ files with added software-generated sleep stage annotations from Beacon Biosignals via the provided secure file transfer system.	Sleep Profiler will operate on any personal computer with Windows XP operating system and at least 2 GB of RAM. The speed by which a study will process is dependent on the computer processor and the amount of RAM	Web-based software operates in the cloud with Windows, Mac OS, or Linux	The subject device requires that the user has a computer to send/receive EDFs to/from Beacon Biosignals. The predicate and reference devices are software that are directly operated by the user.
Cybersecurity	Software operates within infrastructure that requires user authentication, encryption of data at-rest and in-transit, checksum verifications, and access controls.	The person installing the Java applet must have administrator privileges. User must have rights to the account and group to access data via the portal The firewall is not configured to prevent input or output	User authentication with strong password, authorization, end to end SSL encryption, access controls, checksum, network and database controls, intrusion prevention system, and anonymization.	Similar. SleepStageML operates within infrastructure that implements cybersecurity measures similar to the measures implemented for the predicate and reference devices.

		communication with access to the server via ports 22 and 30-29		
Predetermined Change Control Plan (PCCP)	Includes PCCP that allows for update of the signal preprocessing, machine learning model, probability post-processing, and signal quality check.	No PCCP	No PCCP	Predicate and reference devices do not include a PCCP.

Summary of Tests

Beacon Biosignals conducted the necessary non-clinical testing and clinical validation testing of SleepStageML with results supporting the determination of substantial equivalence. Activities that were conducted included the following:

- Software verification testing which included software code reviews, automated testing, acceptance testing, labeling review, cybersecurity and data protection, which confirmed that all software requirements are developed as expected.
- Design validation testing which simulated the intended use to confirm that the end-to-end functionality of SleepStageML meets the design requirements.
- Study that utilized clinical data to demonstrate automatic scoring sleep study performance.
- Design traceability confirming that all requirement tracing is complete from design inputs to verification/validation and that all risk controls are implemented and effective.

Non-Clinical Tests

Support for the substantial equivalence of SleepStageML was provided by requirements verification, risk management and software testing, at the unit, integration, and system levels. Unit and integration tests verify the functionality for individual software parts; and system-level integration tests cover each specified requirement. System level tests were defined with detailed protocols and objective pass/fail criteria and were clearly documented with test execution results for review. SleepStageML passed all unit, integration, and system level testing demonstrating that all requirements were verified and validated.

Clinical Validation Test

The efficacy of SleepStageML was established through a retrospective pivotal validation study using previously collected clinical polysomnography (PSG) recordings from a representative set of 100 patients. Recordings for inclusion in the validation data set were randomly selected from three level 1 clinical PSG data sources and were required to (1) have all EEG channels recommended by the American Academy of Sleep Medicine (AASM), (2) have EEG sampling rates between 128 and 512Hz, (3) have a recording duration between 4 and 24 hours, and (4) be from patients of least 18 years of age, The included patients spanned a variety of ages (between 19 and 83), were balanced across sex (46 female and 54 male) and were stratified across clinical apnea categories (25 patients in each category, normal (AHI < 5), mild (5 ≤ AHI < 15), moderate (15 ≤ AHI < 30), and severe (AHI > 30)).

Each PSG recording was manually and independently sleep staged by three (3) registered PSG technologists (RPSGTs) each with at least 5 years of experience in clinical scoring of

sleep studies. To ensure that the sleep staging outputs obtained from the experts were of sufficient quality, several data-quality and consistency checks were performed. SleepStageML software performance was evaluated against the expert consensus sleep stages that were constructed using 2/3 majority scoring (i.e., the stage per epoch where at least 2 of the 3 experts agree).

Objective performance targets and acceptance criteria of positive agreement (PA), negative agreement (NA), and overall agreement (OA) were predefined to demonstrate non-inferiority to the identified predicate device, Sleep Profiler (K153412). These metrics were computed for all 30-second epochs that had an expert consensus sleep stage (excluding epochs where all 3 RPSGTs disagreed) after pooling across all recordings in the study.

Table 1 shows the SleepStageML clinical performance results as compared to the predicate reported results. Comparing the 95% bootstrapped confidence intervals and mean values to the reference values indicates that SleepStageML is non-inferior to the predicate device. Therefore, the results confirm that the positive, negative, and overall agreement performances of SleepStageML are substantially equivalent to those of Sleep Profiler (K153412), respectively.

TABLE 1: SLEEPSTAGEML CLINICAL PERFORMANCE RESULTS

Sleep Staging Comparisons		SleepStageML vs 2/3 Consensus Sleep Staging Performance				Sleep Profiler (K153412) vs 2/3 Consensus Sleep Staging Performance			
		N=100 subjects	Percent Agreement (%) with 95% percentile bootstrap confidence interval (N=5000 resamples)			N=43 subjects	Point-estimate of Percent Agreement (%)		
			Total Epochs	Overall Agreement (OA)	Positive Agreement (PA)		Negative Agreement (NA)	Total Epochs	Overall Agreement (OA)
Overall epochs using 2/3 consensus scoring	W	21,668	96.1% (95.4%, 96.8%)	88.9% (86.5%, 91.2%)	98.5% (98.2%, 98.8%)	7,424	89%	73%	94%
	N1	3,877	94.5% (93.7%, 95.2%)	58.4% (54.2%, 62.4%)	96.2% (95.4%, 96.9%)	1,752	89%	25%	93%
	N2	42,587	87.1% (85.9%, 88.3%)	79.8% (77.7%, 81.8%)	94.2% (93.2%, 95.0%)	12,582	81%	77%	84%
	N3	6,210	92.9% (91.8%, 93.8%)	93.0% (89.8%, 95.7%)	92.9% (91.7%, 93.9%)	4,704	91%	76%	94%
	R	12,641	97.3% (96.7%, 97.9%)	93.1% (91.5%, 94.5%)	98.0% (97.3%, 98.6%)	3,749	95%	74%	97%
	Total	86,983	Multi-stage Agreement: 84.02%	—	—	31,361	—	—	—
	No Consensus	2,289	—	—	—	1,150	—	—	—

Conclusion

Non-Clinical verification, validation, and clinical validation testing were conducted in accordance with FDA guidance recommendations to confirm the device design meets all specifications and user needs. SleepStageML has passed all software verification and validation tests and its clinical validation testing results demonstrated effective performance and non-inferiority to predicate device's performance. It is therefore concluded that SleepStageML is substantially equivalent to the predicate device.

Predetermined Change Control Plan

SleepStageML includes an authorized Predetermined Change Control Plan (PCCP) that allows for planned updates of the machine learning software device function (ML-DSF) and non-ML algorithmic components to improve sleep staging performance within the existing intended use and indications for use. This PCCP allows for the modification of the algorithmic components of SleepStageML including the signal preprocessing, machine learning model, postprocessing, or signal quality check to achieve increased sleep staging performance. The four modifications are summarized in Table 2 below.

TABLE 2: SUMMARY OF PCCP MODIFICATIONS

#	Modification	Description
1	Update of Machine Learning Model	<p>SleepStageML's sleep staging neural network may be modified for the purposes of improving sleep staging performance within the intended use population by:</p> <ul style="list-style-type: none"> Retraining with an updated training/tuning dataset Retraining with updated hyper-parameters, loss function, optimizer Retraining with updated model selection criteria Retraining with an updated neural network architecture with limitations on model size and type
2	Update of Signal Preprocessing Steps	<p>SleepStageML's EEG signal preprocessing may be modified for the purposes of improving sleep staging performance within the intended use population by:</p> <ul style="list-style-type: none"> Updating the parameters of the digital signal processing steps (e.g., filtering) applied to the EEG signals before being input to the machine learning model
3	Update of Probability Postprocessing	<p>SleepStageML's probability postprocessing may be modified for the purposes of improving sleep staging performance within the intended use population by:</p> <ul style="list-style-type: none"> Updating the methods by which sleep stages are generated from the model output sleep stage probabilities
4	Update of Signal Quality Check	<p>SleepStageML's signal quality check component may be modified for the purposes of improving sleep staging performance within the intended use population by:</p> <ul style="list-style-type: none"> Updating the criteria/thresholds used to check that the input EEG signals are analyzable

Modifications 1 and 2 above would trigger re-training of the machine learning model, while modifications 3 and 4 would not trigger re-training of the machine learning model.

The testing of any modification to SleepStageML within the scope of the PCCP will include comprehensive software verification and validation testing, including repeating all unit, integration, and system level tests performed in the development for the original

SleepStageML software. All software verification tests linked to requirements and specifications must pass for a modification to be considered valid. In addition, clinical performance validation will also be repeated and will require that the performance of any modification to SleepStageML to be non-inferior in per-stage performance metrics to both the original SleepStageML device and its predicate device. In addition, the performance of any modification to SleepStageML must also be non-inferior to the best performance among released versions of SleepStageML with respect to the multi-stage agreement. The acceptance criteria for the clinical performance validation are summarized in the Table 3 below, as well as the modifications for which each criterion is required to pass.

TABLE 3: SUMMARY OF PCCP CLINICAL VALIDATION ACCEPTANCE CRITERIA

Acceptance Criteria	Modifications that require passing this criterion
The per-stage overall, positive, and negative agreements of the modified SleepStageML, as compared to human expert consensus, is non-inferior to both the Original SleepStageML and the predicate device for full overnight recordings.	1, 2, 3, 4
The percentage of human scorable recordings that are unanalyzable by the updated SleepStageML is less than or equal to a predefined threshold.	4
The per-stage overall, positive, and negative agreements of the modified SleepStageML, as compared to human expert consensus, is non-inferior to both the Original SleepStageML and the predicate device for 2-hour recording segments.	1, 2, 3, 4
The per-stage overall, positive, and negative agreements of the modified SleepStageML, as compared to human expert consensus, is non-inferior to both the Original SleepStageML and the predicate device for recordings with the minimum number of AASM recommended EEG channels.	1, 2, 3, 4
The overall multi-stage agreement (across all 5 sleep stages) of the modified SleepStageML is non-inferior to the highest overall multi-stage agreement across all released versions of SleepStageML.	1, 2, 3, 4

Upon a release of an updated version of SleepStageML based on this PCCP, communication will be sent to all external clinical users of SleepStageML, informing them that a new version of SleepStageML is available, with a description of the release and its updated performance.