DE NOVO CLASSIFICATION REQUEST FOR
NEUROPSYCHIATRIC EEG-BASED ASSESSMENT AID FOR ADHD (NEBA) SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Neuropsychiatric Interpretive Electroencephalograph Assessment Aid. The Neuropsychiatric Interpretive Electroencephalograph Assessment Aid is a prescription device that uses a patient's electroencephalograph (EEG) to provide an interpretation of the patient's neuropsychiatric condition. The Neuropsychiatric Interpretive EEG Assessment Aid is used only as an assessment aid for a medical condition for which there exists other valid methods of diagnosis.

NEW REGULATION NUMBER: 882.1440

CLASSIFICATION: CLASS II

PRODUCT CODE: NCG

BACKGROUND

DEVICE NAME: NEUROPSYCHIATRIC EEG-BASED ASSESSMENT AID FOR ADHD (NEBA) SYSTEM

SUBMISSION NUMBER: K112711

DATE OF DE NOVO: DECEMBER 8, 2011

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REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS II

INDICATIONS FOR USE

The Neuropsychiatric EEG-Based ADHD Assessment Aid (NEBA®) uses the theta/beta ratio of the EEG measured at electrode CZ on a patient 6-17 years of age combined with a clinician's evaluation to aid in the diagnosis of ADHD.

NEBA should only be used by a clinician as confirmatory support for a completed clinical evaluation or as support for the clinician's decision to pursue further testing following a clinical evaluation. The device is NOT to be used as a stand-alone in the

evaluation or diagnosis of ADHD.

LIMITATIONS

For prescription use only.

The NEBA cannot be used in an individual for whom an EEG recording is not valid, specifically a patient with:

- a history of EEG abnormalities;
- a history of a seizure disorder;
- on anticonvulsant medication(s);
- a metal plate in the head; or
- a metal device in the head.

The NEBA system cannot be used in subjects who are unable to remain still for a minimum of 30 seconds for EEG recording.

The NEBA system should only be used by medical professionals qualified to assess psychiatric disorders and experienced in diagnosing ADHD. To ensure proper device performance, the user must first perform a diagnostic evaluation per the standard of their practice. NEBA interpretations are based on the clinician's initial diagnostic evaluation, the subject's age and the EEG results.

The device should not be used as a stand-alone diagnostic device.

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

DEVICE DESCRIPTION

The NEBA System consists of the following high-level sub-systems:

1. Compact EEG (CEEG) recording system
2. EEG data archive and communications system (EDACS)
3. NEBA Analysis System (NAS).

The CEEG Recording System is used to acquire EEG data from the patient and consists of a dedicated portable computer and monitor (CEED Computer), EEG amplifier hardware (CEEG Amplifier), and EEG recording software (CEEG Software). EEG data is collected by the CEEG Recording System using FDA cleared electrodes and electroconductive gel. The International 10-20 System is used as a basis for electrode placement. A single recording electrode is placed on the scalp at location CZ, while the ground electrode is placed a location FZ (midline frontal) and linked ears reference. Electrooculography (EOG) is used to monitor eye blinks and gross eye movement.

The EDACS is used to provide secure transmission and storage for training and patient data collected at remote sites and consists of server hardware and software and data

storage. Data collected from the CEEG System is securely transmitted via EDACS to secure storage.

The NAS is stand-alone software which takes in EEG data recorded by the CEEG system, processes it, and produces the final NEBA Report. The NAS consists of EEG artifact reduction and review software, EEG Frequency Analysis and theta-beta ratio calculation software, and the NEBA Report Generator software. Trained technicians first use the NAS to perform manual and algorithm-based artifact reduction of the EEG signal. The artifact-reduced EEG data is then processed using frequency spectrum analysis software, which converts the time-domain EEG data into the frequency domain. Calculations are then performed to determine the ratio of the power of the theta band ([redacted] Hz) to the beta band ([redacted] Hz). Finally, the results of the theta-beta ratio calculations are processed by the NEBA Report Generator to generate the report provided to the clinician.

The high-level NEBA sub-systems form an EEG recording and analysis system that is used to compare an individual's quantified EEG with clinical reference values. NEBA provides clinicians with a specific EEG marker of activity in the form of a power ratio. This ratio is computed by [redacted] Age-adjusted TBR cutoffs are provided that are specific to the NEBA processing and analysis of EEG.

The NEBA interpretive report is transmitted back to the clinician's office and offers two general possibilities that depend on the combination of the NEBA result with the clinician's initial evaluation:

- Confirmatory support
- Further clinical testing may be needed (possible/probable presence of complicating conditions)

Specifically, the interpretative reports may consist of the following:

1. Along with a clinical diagnostic evaluation, NAS will separate the patients with ADHD as the primary clinical diagnosis into two groups:
    a. A group receiving confirmatory support for presence of ADHD as primary diagnosis.
    b. A group receiving support for the clinician's decision to pursue further testing with focus on other conditions before proceeding with ADHD as primary diagnosis.

2. Along with a clinical diagnostic evaluation, NAS will separate patients with an uncertain clinical diagnosis regarding ADHD into two groups:
    a. A group receiving support for the clinician's decision to pursue further testing with focus on ADHD.
    b. A group receiving support for the clinician's decision to pursue further testing with focus on other conditions.

3. Negative for ADHD as the primary clinical diagnosis is always solely determined by the clinician; no ADHD primary diagnosis is possible without the clinician's determination of ADHD.

The following table displays general interpretations delineated by a combination of the clinician's evaluation (ADHD primary diagnosis) and the NEBA result (TBR level). Uncertain zones are highlighted in gray. The uncertain zone for the NEBA result is labeled "moderate" for TBR level.

		NEBA Result		
		Low TBR	**Moderate TBR**	**High TBR**
Clinician's ADHD Evaluation	**Positive for ADHD**	*Strongly Recommend Further Clinical Testing. (other conditions)*	*Suggest Further Clinical Testing. (other conditions)*	*Confirmatory Support for ADHD as primary diagnosis*
	Uncertain for ADHD	*Strongly Recommend Further Clinical Testing. (other conditions)*	*Suggest Further Clinical Testing. (other conditions)*	*Suggest Further Clinical Testing. (ADHD)*
	Negative for ADHD	*Negative for ADHD as primary diagnosis*	*Negative for ADHD as primary diagnosis*	*Negative for ADHD as primary diagnosis*

NEBA cutoffs for analysis were pre-established in a separate study and are different for adolescents (aged 12.00 – 17.99 years) and children (aged 6.00 – 11.99 years):

BIOCOMPATIBILITY/MATERIALS

The conductive media packaged as part of the NEBA system are NuPrep gel, previously cleared under K885306 and Ten20 conductive paste, previously cleared under K883149. The electrodes provided with the compact EEG (CEEG) Recording System are manufactured and procured from Electro-Cap International, Inc., previously cleared under K112319. Since the electrodes and gels have all been cleared previously and from a biocompatibility perspective these uses are consistent with their uses as part of the NEBA system, no new biocompatibility information was necessary to support this *de novo*.

SHELF LIFE/STERILITY

The NEBA system is not provided sterile nor are any of the components to be sterilized by the end user. Cleaning and maintenance instructions for template cleaning and electrode cleaning are included in the labeling.

The sponsor supplies the user with reusable electrodes cleared in K112319, which provides cleaning instructions to the end user.

Neither the NEBA system nor any of its components have a stated shelf life as the products are not provided sterile. Based on the nature of the system components, the absence of a shelf life is acceptable.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The CEEG device was tested against and passed the following EMC, electrical, mechanical, and thermal safety tests:

Standard	Name
IEC60601-1 (Second Edition)	Medical Electrical Equipment; Part 1: General Requirements for Safety
UL 60601-1	Medical Electrical Equipment, Part 1: General Requirements for Safety (based on IEC second edition, with U.S. national differences)
IEC60601-1-1	Medical electrical equipment; Part 1-1: General Requirements for Safety - Collateral standard: Safety requirements for medical electrical system.
IEC60601-2-26	Medical Electrical Equipment Part 2-26: Particular Requirements for the Safety of Electroencephalographs
CSA C22.2 No. 601.1-M90 CAN/CSA C22.2 NO. 601.1-M90 (R2005)	Medical Electrical Equipment - Part 1: General Requirements for Safety, Canadian Standards Association / National Standard of Canada / 01 Nov-1990
IEC60601-1-2	Medical electrical equipment; Part 1-2: General Requirements for Safety - Section 2: Collateral standard: Electromagnetic compatibility - Requirements and tests.
IEC60601-1-4	Medical Electrical Equipment; Part 1-4: General Requirements for Safety - Collateral Standard. Programmable Electrical Medical Systems.
IEC/UL 60950-1	Information technology equipment - Safety - Part 1: General requirements.
ISO 14971 (2000)	Medical devices; Application of Risk Management to Medical Devices
ISO 13485: 2003	Medical devices - Quality management systems - Requirements for regulatory purposes

SOFTWARE

Software for the device consisted of both proprietary software and off-the-shelf (OTS) software. The software was reviewed and the provided documentation was found adequate and consistent with a 'MODERATE' level of concern., as discussed in the FDA document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005.

PERFORMANCE TESTING – BENCH

The sponsor provided thorough bench testing in K112711 which were all considered to be adequate. All three main systems in the NEBA System were tested:

1. Compact EEG (CEEG) recording system, the physical hardware used to acquire the EEG data;
2. EEG data archive and communications system (EDACS), software used to provide secure transmission for EEG data collected at remote sites
3. NEBA Analysis System (NAS), software used to analyze the EEG data and generate NEBA reports

This testing included sub-system verification of each component within the system, followed by system-level integration testing to test the components working together as a complete system. The non-clinical tests were performed prior to commencing clinical validation studies.

Non-clinical testing included verification testing of the following:

- noise performance
- analog-to-digital converter (ADC) quantization and resolution
- input impedance between leads
- common mode rejection ratio (CMRR)
- power supply rejection ratio
- impedance measurement and display
- filtering and signal processing
- electrical performance and filtering, including:
  - sampling rate
  - harmonic distortion
  - absolute signal amplitude
  - inter-channel crosstalk
- re-sampling and anti-aliasing
- amplitude accuracy and precision
- frequency response
- time domain representation and signal morphology
- theta-beta ratio calculations
- threshold artifact
- Fast Fourier Transform (FFT) calculations
- software security / cyber security

Additionally, software verification and validation testing was provided and determined adequate for a software with a 'MODERATE' level of concern, in accordance with the FDA document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005. Software verification and validation also included evaluation of software security / cybersecurity.

SUMMARY OF CLINICAL INFORMATION

1. Clinical Study Design

   The objective of the study was to evaluate the diagnostic clinical performance of the NEBA system according to the intended use and to evaluate the repeatability of the NEBA measure (EEG theta/beta ratio). The clinical investigation included an initial study and an extension of that study, including:

   a. Study 1 – Collection of EEG and clinical evaluation data.
   b. Study 2 – Multidisciplinary team review of clinical evaluation data from Study 1 to determine consensus best estimate diagnosis for attention deficit hyperactivity disorder.

   Subjects were children (aged 6.00-11.99 years) and adolescents (aged 12.00-17.99 years) who consecutively presented with attention and/or behavioral concerns to 13 geographically distinct clinics (5 Pediatric, 3 Psychological, and 5 Psychiatric) in the US. Recruited subjects on medications required a washout plan determined and monitored by the site investigator. In the protocol, washout of at least one week or longer was recommended, but depended on the medication and the clinician's judgment. Washout recommendations in the protocol included: 1) psychostimulants at least one week prior to entering the study, 2) other psychiatric medications at least two weeks prior to entering the study, and 3) Fluoxetine 28 days prior to study entry. Of the 275 subjects included in the final analysis, 13 (5%) required medication washout prior to study entry. No adverse effects related to medication withdrawal were reported over the course of the clinical investigation. Of 364 subjects recruited, there were 275 subjects who met protocol criteria, completed the study, and had complete EEG recordings. All of the 275 subjects were included in the analysis of diagnostic clinical performance.

   In Study 1, investigators conducted a prospective, double-blinded, multi-site, clinical cohort study. Over the course of 3 visits, investigators collected comprehensive clinical evaluation data used later for best estimate diagnosis in Study 2. Clinical evaluation data included a clinician's interview based on the DSM-IV-TR criteria, a semi-structured clinical interview, behavior rating scales, IQ and achievement testing, scales of severity and dysfunction, a physical exam, hearing and visions screens, medical/neurological/medication histories, questionnaire on socioeconomic status/education/family history, and any further testing if deemed necessary by the clinician. Using these data, the clinicians performed diagnostic evaluations for ADHD and other conditions and disorders. In a double-blinded protocol, separate groups of investigators collected NEBA data (EEG). The blind-break was handled by an independent third party vendor. Prior to blind-break, NEBA data, clinical evaluation data, and clinician's diagnostic results were monitored, entered into databases, and locked.

Study 2 was a prospectively planned retrospective review of de-identified patient files from Study 1 by a multidisciplinary clinical team to determine a consensus best estimated diagnosis for ADHD and other disorders and conditions. The multidisciplinary clinical team was comprised of a clinical psychologist, a neurodevelopmental pediatrician, and a child/adolescent psychiatrist. The patient files included all clinical evaluation data from Study 1, except for blinding to NEBA results, parent rating scales, and clinician diagnostic conclusions.

Interpretation result for each subject was determined from the results of the locked databases of Study 1, specifically using the NEBA data (EEG) and the clinician diagnostic conclusions. To evaluate performance, the NEBA Interpretation results from Study 1 were compared with the best estimate diagnosis results by consensus of the multidisciplinary team from Study 2.

2. Clinical Performance Results.

The diagnosis of ADHD (clinical reference standard) was based upon the best estimate diagnosis (BED) results by consensus of the multidisciplinary team from Study 2 which reviewed all clinical assessments and were blinded to the NEBA results. The classification of results for NEBA Interpretation (NEBA+Clinician's initial diagnosis) per the intended use for each age category are provided in the Tables below. Clinical sensitivity and specificity of the NEBA interpretation results were calculated by combining NEBA interpretation results 'Further Testing for ADHD' with 'ADHD' to provide 'NEBA interpretation positive' and by combining NEBA interpretation results 'Further Testing for Other Condition' with 'Other Condition' to provide 'NEBA interpretation negative'.

Table 1 ADOLESCENTS (aged 12.00-17.99 years)**.** Classification of results for NEBA Interpretation (NEBA+Clinician's initial diagnosis) versus best estimate diagnosis results (BED) from the multidisciplinary team

		BED		
		ADHD or 'Further Testing for ADHD is supported'	Other Condition or 'Further Testing for Other Conditions is supported'	Total
NEBA Interpretation	ADHD	22	5	27
	Further Testing (ADHD)	3	1	4
	Further Testing (Other Conditions)	2	32	34
	Other Condition	1	8	9
	Total	28	46	74

Table 2 - ADOLESCENTS. Performance results for NEBA Interpretation

	Estimate	95% Confidence Interval
Specificity (%)	87% (40/46)	(74%, 94%)
Sensitivity (%)	89% (25/28)	(73%, 96%)

PPV (%)	81% (25/31)	(64%, 91%)
NPV (%)	93% (40/43)	(81%, 98%)
Overall Concordance (%)	88% (65/74)	(78%, 93%)

For PPV (positive predictive value) and NPV (negative predictive value) reference, the study prevalence of the positive condition (ADHD) was 38% (28/74) and of the negative condition (condition other than ADHD) was 62% (46/74).

Table 3 – CHILDREN (aged 6.00-11.99 years)**.** Classification of results for NEBA Interpretation (NEBA+Clinician's initial diagnosis) versus best estimate diagnosis results (BED) from the multidisciplinary team

		BED		
		ADHD or 'Further Testing for ADHD is supported'	Other Condition or 'Further Testing for Other Conditions is supported'	Total
NEBA Interpretation	ADHD	73	3	76
	Further Testing (ADHD)	8	0	8
	Further Testing (Other Conditions)	19	77	96
	Other Condition	2	19	21
	Total	102	99	201

Table 4 - CHILDREN. Performance results for NEBA interpretation

	Estimate	95% Confidence Interval
Specificity (%)	97% (96/99)	(91%, 99%)
Sensitivity (%)	79% (81/102)	(71%, 86%)
PPV (%)	96% (81/84)	(90%, 99%)
NPV (%)	82% (96/117)	(74%, 88%)
Overall Concordance (%)	88% (177/201)	(83%, 92%)

For PPV (positive predictive value) and NPV (negative predictive value) reference, the study prevalence of the positive condition (ADHD) was 51% (102/201) and of the negative condition (condition other than ADHD) was 49% (99/201).

The results demonstrated a negative predictive value (NPV) of 93% in adolescents and 82% in children as compared to the study prevalence for other condition (negative) of 62% in adolescents and 49% in children who present with attention and behavior concerns.

Accordingly, a negative NEBA interpretation result (other condition) supports further testing for other conditions before proceeding with ADHD as primary diagnosis. The results also demonstrated a positive predictive value (PPV) of 81% in adolescents and 96% in children as compared to the study prevalence for ADHD (positive) of 38% in adolescents and 49% in children who present with attention and behavior concerns. Accordingly, a positive NEBA interpretation result (ADHD) provided confirmatory support for ADHD as primary diagnosis.

When comparing the performance of NEBA Interpretation (clinician using NEBA) versus clinician alone against the clinical reference standard, the results indicate that NEBA provides additional information beyond the clinician's initial diagnosis, substantiating the use of NEBA. A comparison of classification results for the clinician's initial diagnosis alone without NEBA versus NEBA Interpretation (NEBA+Clinician's initial diagnosis) per the intended use for each age category are provided in the Tables below:

Table 5 - ADOLESCENTS

	BED = ADHD or 'Further Testing for ADHD is supported'				
		Clinician alone			
		ADHD	Uncertain	Other Condition	Total
NEBA Interpretation*	positive	22	3	0	25
	negative	2	0	1	3
	Total	24	3	1	28

	BED = Other Condition or 'Further Testing for Other Conditions is supported'				
		Clinician alone			
		ADHD	Uncertain	Other Condition	Total
NEBA Interpretation*	positive	5	1	0	6
	negative	20	12	8	40
	Total	25	13	8	46

*NEBA Interpretation is NEBA+Clinician's initial diagnosis per the intended use. NEBA interpretation 'positive' combines NEBA interpretation results 'Further Testing for ADHD' with 'ADHD'; and, NEBA interpretation 'negative' combines NEBA interpretation results 'Further Testing for Other Condition' with 'Other Condition'.

Table 6 - CHILDREN

	BED = ADHD or 'Further Testing for ADHD is supported'				
		Clinician alone			
		ADHD	Uncertain	Other Condition	Total
NEBA Interpretation*	positive	73	8	0	81
	negative	19	0	2	21
	Total	92	8	2	102

	BED = Other Condition or 'Further Testing for Other Conditions is supported'	

		Clinician alone			
		ADHD	Uncertain	Other Condition	Total
NEBA Interpretation*	positive	3	0	0	3
	negative	65	12	19	96
	Total	68	12	19	99

*NEBA Interpretation is NEBA+Clinician's initial diagnosis per the intended use. NEBA interpretation 'positive' combines NEBA interpretation results 'Further Testing for ADHD' with 'ADHD'; and, NEBA interpretation 'negative' combines NEBA interpretation results 'Further Testing for Other Condition' with 'Other Condition'.

3. Precision of NEBA Measure (EEG theta/beta ratio). The repeatability (test-retest reliability) of the NEBA theta/beta ratio (TBR) was estimated from two sets of EEG data for each patient recorded on different days (approximately 2 ½ weeks apart on the average). There were 198 patients with two sets of EEG data available for this analysis. The intraclass correlation coefficient (ICC) of repeated NEBA TBR was 0.83.

   The repeatability (variability between duplicate results) was estimated as the pooled standard deviation (SD) between duplicate TBR results across subjects. Repeatability SD increases from low to high TBR; therefore, SDs for different TBR groups are stratified in the table below to reflect the non-constant variability across the range of TBR results.

   Table 7. Standard deviation estimated from paired TBR measurements.

TBR range	n	Standard Deviation Estimated from Paired Measurements
0.00 to 3.00	47	0.42
3.01 to 4.50	60	0.76
4.51 to 7.50	72	1.01
> 7.50	19	1.55

4. Conclusions.
   a. NEBA performance has been established by the results of the clinical investigation.
      i. An ADHD patient with a NEBA interpretation result of "confirmatory support" is likely to have ADHD as primary diagnosis (adolescents: PPV=81%, prevalence=38%; children: PPV=96%, prevalence=51%).
      ii. An ADHD patient with a NEBA interpretation result of "further testing" is likely to have complicating conditions that might have an impact on the clinician's decision regarding ADHD as primary diagnosis (adolescents: NPV=93%, prevalence=38%; children: NPV=82%, prevalence=51%; 7 significant OR results for complicating conditions; 4 further significant OR results in support of further testing).
   b. The NEBA measure, theta/beta ratio, can be reliably determined in the intended use population (ICC=0.83). NEBA test-retest results were stable and represented a

strong correlation (≥0.7); and met general recommendations for psychological testing (≥0.6) .

c. NEBA safety has been established. Physical use of the device has been shown to be safe. EEG collection is a non-invasive procedure. No adverse device events and no unanticipated adverse device events were reported in the clinical investigation.

LABELING

The *NEBA System User Manual* and *NEBA Compact EEG System User Manual* are consistent with the clinical data and cover all the hazards and other clinically relevant information that may impact use of the device (see *NEBA System User Manual* and *NEBA Compact EEG System User Manual*). The labeling is sufficient and satisfies the requirements of 21 CFR § 801.109 Prescription devices. The following labeling issues with respect to the NEBA System include:

1. A warning that the device is not to be used as a stand-alone diagnostic.
2. A detailed summary of the clinical performance testing, including any adverse events and complications.
3. The qualifications and training requirements for device users including technicians and clinicians.
4. The intended use population and the intended use environment.
5. Labeling must address any instructions technicians should convey to patients regarding the collection of EEG data.
6. Information allowing clinicians to gauge clinical risk associated with integrating the EEG-based measure of ADHD into their diagnostic pathway.
7. Where appropriate, validated methods and instructions for reprocessing of any reusable components.

The safety characteristics and intended purpose of the device requires training of the end-user as follows (see also *NEBA System User Manual*). Clinicians utilizing the NEBA Report should be medical professionals with expertise in the assessment of psychiatric disorders and must have familiarized themselves with all the manuals and labeling of the NEBA System. Technicians operating the Compact EEG (CEEG) recorder must be trained and certified by NEBA Health, LLC prior to operation of the CEEG recorder component.

Warnings include that the clinician must ensure that standard EEG practices are followed in the collection of patient data.

SPECIAL CONDITIONS FOR USE

NEBA interpretation guidelines are based on the clinician's initial diagnostic evaluation, the subject's age and the EEG results. The device user refers to the individual who prescribes device use and performs the initial diagnostic assessment. In order to use the NEBA System, the user should be medical professionals with expertise in the assessment of psychiatric disorders and must have familiarized themselves with all the manuals and labeling of the NEBA System. The clinician must perform a diagnostic evaluation per the standard of their practice. The clinician's evaluation separates the patients into three groups: 1) ADHD is primary diagnosis, 2) uncertain

for ADHD as primary diagnosis, and 3) other condition is primary diagnosis. To generate a NEBA Report, the technician or clinician submits to NEBA Health the clinician's initial clinical evaluation result for ADHD primary diagnosis along with the EEG collected from the patient. NEBA Health generates and returns a NEBA Report based on validated NEBA interpretation guidelines.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of Neuropsychiatric Interpretive Electroencephalograph Assessment Aids and the measures necessary to mitigate these risks.

Identified Risk	**Mitigation Measure**
Adverse Tissue Reaction	Biocompatibility Labeling
Electromagnetic Incompatibility	Electromagnetic Compatibility Testing
Equipment Malfunction Leading to Injury to User/Patient (shock, burn, or mechanical failure)	Electrical safety, thermal, and mechanical testing Labeling
False Result Leading to Delay in Treatment or Unnecessary Treatment due to Hardware Failure	Performance testing Hardware and Software verification, validation and hazard analysis Technical parameters Labeling
False Result due to Incorrect Artifact Reduction	Operator training Software verification and validation Labeling
False Result due to Incorrect Placement of Electrodes	Operator training Clinical performance testing Labeling
False Result when a Neuropsychiatric Interpretive EEG Assessment Aid is used for Confirmatory Support or Support for Further Testing	Clinical performance testing Device design characteristics Labeling
Use error	Clinical performance testing Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the Neuropsychiatric Interpretive Electroencephalograph Assessment Aid is subject to the following special controls:

1. The technical parameters of the device, hardware and software, must be fully characterized and must demonstrate a reasonable assurance of safety and effectiveness.

a. Hardware specifications must be provided. Appropriate verification, validation and hazard analysis must be performed.
b. Software, including any proprietary algorithm(s) used by the device to arrive at its interpretation of the patient's condition, must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Appropriate software verification, validation, and hazard analysis must be performed.

2. The device parts that contact the patient must be demonstrated to be biocompatible.
3. The device must be designed and tested for electrical safety, electromagnetic compatibility (EMC), thermal and mechanical safety.
4. Clinical performance testing must demonstrate the accuracy, precision, reproducibility, of determining the EEG-based interpretation, including any specified equivocal zones (cut-offs).
5. Clinical performance testing must demonstrate the ability of the device to function as an assessment aid for the medical condition for which the device is indicated. Performance measures must demonstrate device performance characteristics per the intended use in the intended use environment. Performance measurements must include sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) per the device intended use. Repeatability of measurements must be demonstrated using interclass correlation coefficients and illustrated by qualitative scatter plot(s).
6. The device design must include safeguards to prevent use of the device as a stand-alone diagnostic.
7. The labeling must bear all information required for the safe and effective use of the device, including:
    a. A warning that the device is not to be used as a stand-alone diagnostic.
    b. A detailed summary of the clinical performance testing, including any adverse events and complications.
    c. The qualifications and training requirements for device users including technicians and clinicians.
    d. The intended use population and the intended use environment.
    e. Any instructions technicians should convey to patients regarding the collection of EEG data.
    f. Information allowing clinicians to gauge clinical risk associated with integrating the EEG interpretive assessment aid into their diagnostic pathway.
    g. Where appropriate, validated methods and instructions for reprocessing of any reusable components.

BENEFIT/RISK DETERMINATION

The risks of the device are based on data collected in the clinical study. There were no serious adverse events reported in the clinical performance study. No adverse device events and no unanticipated device reports were reported in the clinical investigation. The risks to health are relatively minimal as EEG is considered a non-invasive medical device. There is a potential risk associated with the requirement that subjects must be washed out of any medication currently being taken to obtain valid EEG recordings. The required wash-out has the potential to exacerbate an existing behavioral condition. However, in the clinical study, no adverse effects of

the wash-out were reported over the course of the clinical investigation. The risk of a false positive result may result in initiating medication therapy for ADHD that is not needed. A false positive result could also potentially delay the treatment of the actual underlying medical condition. The risk of a false negative result may result in delaying treatment for ADHD in a patient while they are receiving further diagnostic evaluations that are not necessary.

The probable benefits of the device are also based on data collected in a clinical study as described above. The NEBA system requires the clinician to initially conduct an evaluation for ADHD. The clinician's diagnostic impression plus the results generated by the NEBA system may reduce the potential for over-diagnosis of ADHD, and thereby reduce the risks of administering unnecessary pharmacologic therapy in the intended use population (children and adolescents, ages 6.00 – 17.99 years). Furthermore, a clinical impression that is negative for ADHD cannot be over-ridden by the NEBA interpretive system, i.e., the NEBA system does not generate an interpretive report if the clinician's diagnosis of ADHD is negative. The NEBA system only provides confirmatory support for a clinical evaluation that is positive for ADHD or the need for further testing for either a positive or uncertain clinical diagnosis.

Additional factors to be considered in determining probable risks and benefits for the NEBA system include: (1) the clinical performance study was a blinded, multi-site controlled clinical trial, (2) the clinical sites represent a relatively broad geographic sample, (3) the clinical determination of ADHD was a comprehensive evaluation and (4) there currently are no legally marketed physiologically-based assessment aids for ADHD.

In conclusion, the data support that for an electroencephalograph-based assessment aid for attention deficit (ADHD) which is intended to be used as an assessment aid that is part of a full psychiatric workup for ADHD, the probable benefits outweigh the probable risks for the NEBA System. The device provides substantial benefits and the risks can be mitigated by the use of general and special controls.

CONCLUSION

The *de novo* for the NEBA System is granted and the device is classified under the following:

Product Code: NCG
Device Type: Neuropsychiatric Interpretive Electroencephalograph Assessment Aid
Class: Class II
Regulation: 21 CFR 882.1440