DE NOVO CLASSIFICATION REQUEST FOR BRAINPULSE, MODEL 1100

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Cranial Motion Measurement Device. A cranial motion measurement device is a prescription device that utilizes accelerometers to measure the motion or acceleration of the skull. These measurements are not to be used for diagnostic purposes.

NEW REGULATION NUMBER: 21 CFR 882.1630

CLASSIFICATION: CLASS II

PRODUCT CODE: POP

BACKGROUND

DEVICE NAME: BRAINPULSE, MODEL 1100

SUBMISSION NUMBER: DEN140040

DATE OF DE NOVO: DECEMBER 23, 2014

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REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS II

INDICATIONS FOR USE

The BrainPulse is intended for use on a patient's head to non-invasively detect, amplify and capture the skull motion caused by pulsatile flow from the cardiac cycle. The BrainPulse is not indicated to aid in the diagnosis of neurological conditions, diseases, or disorders.

LIMITATIONS

For prescription use only.

The BrainPulse is not indicated for use on patients with a wound close to a sensor location.

The position of the subject has an impact on the BrainPulse recording. The recording may

be affected by whether the subject is sitting upright or is supine, whether the head is facing forward or to the side. Changes to the position cause changes to blood flow and this changes brain motion. As a result, if multiple recordings are obtained from the same subject, a consistent position between recordings will lead to more comparable recordings.

Patient respiration rate, heart rate, and head and body motion also may cause variation in the recording. The presence of atrial fibrillation, premature ventricular contractions, stroke, aneurysms, or intracranial bleeding in patients may also cause variations in the recording.

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

DEVICE DESCRIPTION

As described above, the BrainPulse, Model 1100 (BrainPulse) is designed to measure skull motion caused by pulsatile blood flow. The BrainPulse measures these cranial pulsatile movements via an array of accelerometers placed on the scalp. The system consists of three main components: a headset, data collector, and computer.

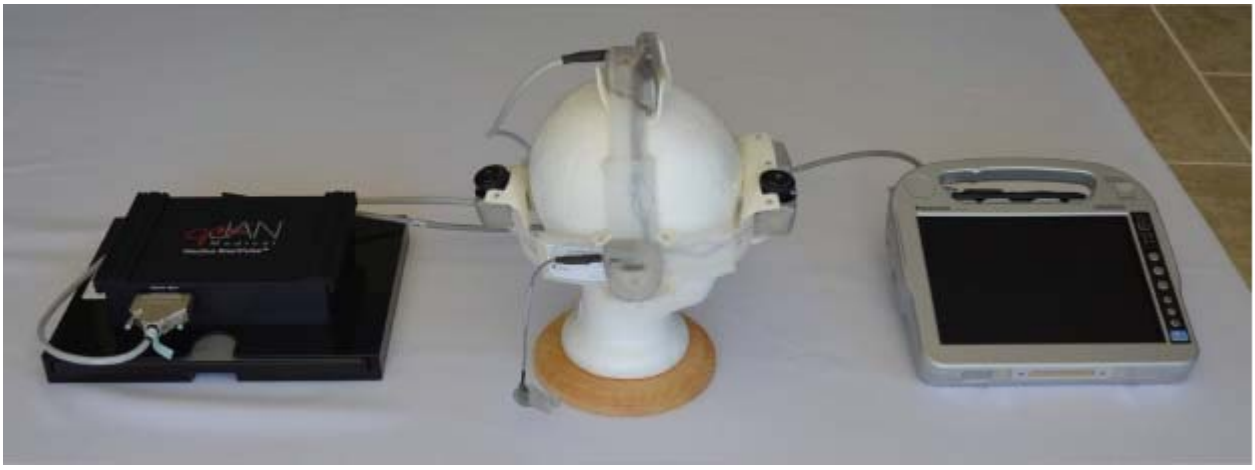

Figure 1. BrainPulse system consisting of the data collector and battery, headset containing sensors, and computer.

The headset contains a forehead photoplethysmograph (PPG) sensor that measures the patient's pulse rate, a Sound Pressure Level (SPL) sensor for detecting ambient environment noise, and six accelerometers to detect the acceleration of the skull at six selected locations. These acceleration measurements typically fall in the range of 0.001 – 0.03 g. See Figure 2 below for a graphical representation of the proper accelerometer placement.

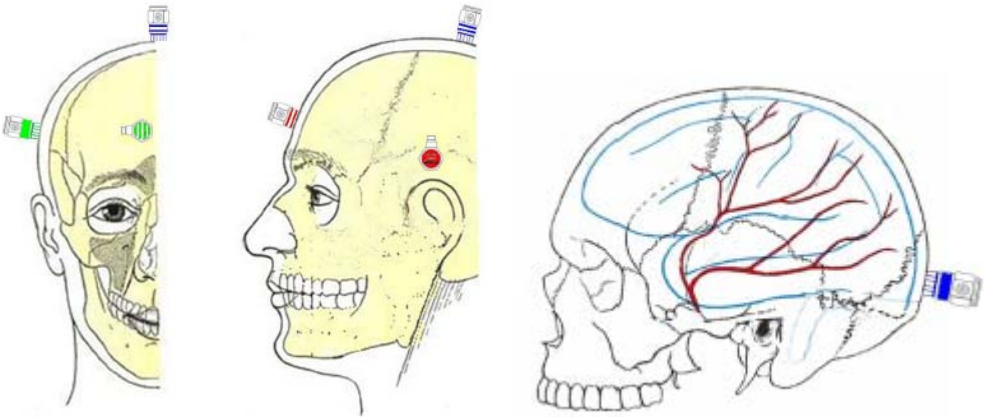

Figure 2. BrainPulse accelerometer placement.

Figure 3. BrainPulse headset viewed from the front (left panel) and from the right (right panel).

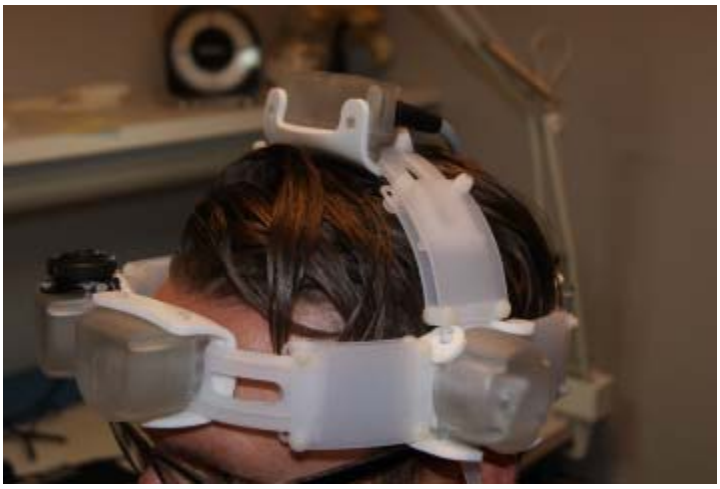

Figure 4. BrainPulse headset worn on a patient's head.

The data collector converts the analog signals from the headset sensors and provides a digital data stream via Ethernet cable to the computer. The computer is loaded with software that allows for the user to initiate and end recordings and to manage saved data files. The BrainPulse software is not capable of displaying the recorded data from the headset; rather the data are saved in multiple file formats that can be readily displayed using other third-party software for post-hoc review. Please refer to Figure 5 below for an example of what the acceleration measurements might look like when plotted using a third-party application.

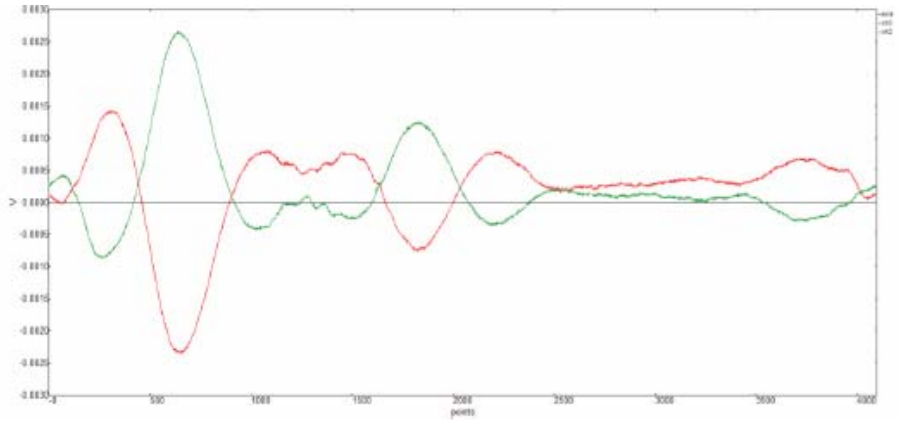

Figure 5. Sample plot of accelerometer data recording from the left and right temple accelerometers for a single heartbeat. This waveform is an average of data recorded across 45 heartbeats.

SUMMARY OF NONCLINICAL/BENCH STUDIES

The sponsor conducted a series of bench testing to demonstrate that the BrainPulse would perform as anticipated. Please refer to the sub-sections below for a discussion of each non-clinical test performed.

BIOCOMPATIBILITY/MATERIALS

The BrainPulse contacts the patient's skin for typically no longer than a 30-minute recording session. The BrainPulse is categorized as a surface-contacting device with a limited duration of contact (less than 24 hours). In accordance with ISO 10993-1:2009, Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing within a Risk Management Process, the following biocompatibility testing was conducted on the BrainPulse. The biocompatibility evaluation was deemed adequate.

Table 1. Biocompatibility testing completed for the BrainPulse

Test	Purpose	Results
Cytotoxicity Evaluation – L929 MEM Elution Test/L929 Neutral Red Uptake Test	To assess the biological activity of L-929 mouse fibroblast cells (grown in culture) after exposure to extracts prepared from the completed BrainPulse system	Non-cytotoxic
Kligman Maximization Test	To estimate the potential for sensitization of the BrainPulse system extract using the guinea pig as an animal model	Sensitization rate = 0% Sensitization grade = "Weak"
Primary Skin Irritation Test	To estimate the potential to produce primary skin irritation after a single topical exposure to the skin of New Zealand White Rabbits	No signs of erythema or edema Considered a Negligible Irritant

Test	Purpose	Results
Intracutaneous Injection Test	To assess the irritating potential of extracts of the BrainPulse system to cause irritation to the exposed part of the body	No difference between mean test article score and mean control score

SHELF LIFE/STERILITY

The BrainPulse is not provided sterile nor are any of the components to be sterilized by the end user. Cleaning and maintenance instructions are included in the device labeling.

The BrainPulse and its components do not have a stated shelf life as the products are not provided sterile. However, the device labeling states that the device has an expected service life of 5 years, which is typical for general electronic devices. Based on the nature of the system components, this estimation of product life is acceptable.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The BrainPulse was tested in accordance with the following consensus standards and passed the following electromagnetic compatibility (EMC), electrical, mechanical, and thermal safety tests:

Table 2. EMC and electrical safety testing completed for the BrainPulse

Standard	Name
IEC60601-1: 2005 +AM1: 2012	Medical Electrical Equipment; Part 1: General Requirements for Safety
IEC60601-1-2: 2007	Medical Electrical Equipment; Part 1-2: General Requirements for Safety - Section 2: Collateral standard: Electromagnetic compatibility - Requirements and tests.

SOFTWARE

Software for the device consisted of proprietary software. The software is 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. Appropriate documentation was provided as part of the *de novo* request.

PERFORMANCE TESTING – BENCH

The BrainPulse was subjected to a series of bench tests to assess its functional performance. These tests were performed on a final manufactured product. Table 3 summarizes the testing performed:

Table 3. Bench testing completed for the BrainPulse

Test	Purpose	Results
Accelerometer Measurement Stability and Repeatability	To ensure acceleration measurements made by the BrainPulse device are stable within a typical recording session	Passed; all within-session recording segments demonstrated stable correlation with a baseline recording. ANOVA results did

Test	Purpose	Results
	and are repeatable across multiple recording sessions and multiple operators	not demonstrate variation in the recordings across multiple sessions or operators
Accelerometer Resolution	To ensure the expected changes in acceleration measured by the BrainPulse device are adequately resolved by the BrainPulse and are above the observed noise floor	Passed; frequency analysis and visual inspection demonstrate signals of interest are resolved above the observed noise floor that confirms accelerometer specifications
PPG Sensor Accuracy and Precision	To ensure the BrainPulse device accurately and precisely measures heartrate based upon changes in blood flow	Passed; visual comparison to concurrent SpO2 (blood oxygen saturation) sensor recordings demonstrate adequate PPG sensor performance
Hardware Verification	To ensure the accelerometers adequately measure acceleration across the range of expected values during intended use of the BrainPulse device	Passed; calibration of accelerometers confirms operation according to specification
	To ensure the Sound Pressure Level (SPL) sensor adequately measures ambient noise across a frequency range relevant to the BrainPulse device and in the intended use environment of the BrainPulse device	Passed; successful measurement of test signals in intended use environment, compared to reference measurement device
	To ensure the Data Collector battery charges and discharges according to specification	Passed; battery operates according to specification
	To ensure the tablet system properly interfaces with the Data Collector and properly records sensor data	Passed; tablet passed all functional requirements

SUMMARY OF CLINICAL INFORMATION

Summaries of six (6) clinical studies (4 completed or terminated, and 2 ongoing) were supplied to support a determination of a reasonable assurance of the safety and effectiveness of the BrainPulse. These studies were conducted both at centers within and outside the United States. While these clinical studies were performed on a wide variety of patient populations with varying neurological conditions, the BrainPulse has only been evaluated in the context of the indications for use; that is, the device's ability to measure cranial motion due to the pulsatile flow from the cardiac cycle.

In total, 616 successful recordings were evaluated from 273 patients across all six of the studies. All studies demonstrated the measured skull motion correlated with a regular pulse related to the cardiac cycle. Only some of the studies obtained multiple recordings per patient; however, no major variations in within-patient recordings were reported. These results were supported by the

stability and repeatability testing summarized in the "Performance Testing – Bench" section above.

Two patients from one of the studies complained of discomfort when wearing the headset. No other adverse events, complaints, or device issues or malfunctions were reported.

LABELING

The user manual is consistent with the performance data and covers all the hazards and other clinically relevant information that may impact use of the device. The labeling satisfies the requirements of 21 CFR § 801.109 Prescription devices. The labeling for the BrainPulse includes:

1. The intended use population and the intended use environment.
2. Instructions technicians should convey to patients regarding the collection of cranial motion data.
3. Information allowing clinicians to understand potential sources of variability in the measurement to help recognize and identify changes in the measurement.

Because cranial motion data are currently not typically included in the clinical evaluation of patients, clinicians utilizing the measurement data provided by the BrainPulse should be physicians who have familiarized themselves with the labeling of the BrainPulse.

RISKS TO HEALTH

Table 4 below identifies the risks to health that may be associated with use of Cranial Motion Measurement Device and the measures necessary to mitigate these risks.

Table 4. Identified Risks to Health and Mitigation Measures

Identified Risk	**Mitigation Measure**
Adverse Tissue Reaction	Biocompatibility Evaluation Labeling
Equipment Malfunction Leading to Injury to User or Patient	Electrical, Mechanical and Thermal Safety Testing Electromagnetic Compatibility Testing Labeling
Inaccurate Measurement	Clinical Performance Testing Hardware and Software verification, validation and hazard analysis Electromagnetic Compatibility Testing Labeling
Use Error	Hardware and Software verification, validation and hazard analysis Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the Cranial Motion Measurement Device is subject to the following special controls:

1. The technical parameters of the device, hardware and software, must be fully characterized and include the following information:
    a. Hardware specifications must be provided. Additionally, verification and validation testing as well as a hazard analysis must be performed.
    b. Software must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Additionally, software verification and validation testing as well as a hazard analysis must be performed.

2. The patient-contacting components of the device must be demonstrated to be biocompatible.

3. The device must be designed and tested for electrical, thermal and mechanical safety and electromagnetic compatibility (EMC).

4. Clinical performance testing must demonstrate the accuracy, precision, stability, and repeatability of measuring cranial motion per the intended use in the intended use environment.

5. The labeling must include:
    a. The intended use population and the intended use environment.
    b. Any instructions technicians should convey to patients regarding the collection of cranial acceleration data to ensure device measurement accuracy, precision, stability, and repeatability.
    c. Information allowing clinicians to understand potential sources of variability in the measurement to help recognize and identify changes in the measurement.

BENEFIT/RISK DETERMINATION

While the summaries of 6 completed, terminated, or ongoing clinical studies were provided, no formal clinical study was provided, requested, or deemed necessary for the BrainPulse based on the risks for the current indications for use. The probable risks of the device are based on risk analysis, bench and clinical testing that included assessments of accuracy and precision, as well as the stability and repeatability studies described above. Probable device-related adverse events include adverse tissue reaction, equipment malfunction leading to injury of the user or patient, inaccurate measurement, and use error leading to inaccurate measurement or patient discomfort. Based on the nonclinical and clinical information provided, the probability of each of these adverse events is low.

The probable benefits of the device are also based on the clinical summaries, bench testing, as well as the stability and repeatability studies described above. The BrainPulse measures skull motion correlated with the cardiac cycle. This measurement is stable and repeatable under

controlled procedures and in a controlled environment, allowing clinicians to observe notable differences or changes in the measurement that may be incorporated into their clinical assessment paradigm. It should be noted that the clinical data were only reviewed in the context of the indications for use; that is, the device's ability to measure skull motion due to the pulsatile flow from the cardiac cycle. Consequently, a demonstration of clinical diagnostic utility in specific patient populations was not required.

Additional factors to be considered in determining probable risks and benefits for the BrainPulse include:

- Skull motion is a physiological measurement that is currently not typically included in the clinical evaluation of patients. Diagnostic utility of this additional physiological data has not been established for specific patient populations.
- Patient respiration rate, heart rate, and head and body motion also may cause variation in the recording. The presence of atrial fibrillation, premature ventricular contractions, stroke, aneurysms or intracranial bleeding in patients may also cause variations in the recording. These sources of variation have been identified through risk analyses and preliminary clinical use; however, additional sources of variability remain unknown.
- Feedback from centers using the device in preliminary clinical studies has been positive in terms of ease of use.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for use on a patient's head to non-invasively detect, amplify and capture the skull motion caused by pulsatile flow from the cardiac cycle, the probable benefits outweigh the probable risks for the BrainPulse. The device provides benefit, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The *de novo* request for the BrainPulse, Model 1100 is granted and the device is classified under the following:

Product Code: POP
Device Type: Cranial Motion Measurement Device
Class: Class II
Regulation: 21 CFR 882.1630