February 17, 2023

Medasense Biometrics Ltd.
℅ Jonathan Kahan
Partner
Hogan Lovells
555 Thirteenth Street NW
Washington, DC 20004

Re: DEN210022
   Trade/Device Name: PMD-200
   Regulation Number: 21 CFR 868.2200
   Regulation Name: Adjunctive pain measurement device for anesthesiology
   Regulatory Class: Class II
   Product Code: QVE
   Dated: June 4, 2021
   Received: June 4, 2021

Dear Jonathan Kahan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the PMD-200, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> The PMD-200 with the Nociception Level (NOL) Index is indicated for use in a clinical setting that requires assessment of changes in nociception levels in adult patients under general anesthesia receiving opioid or opioid-sparing analgesia as part of their care.

> The PMD-200 should be used as an adjunct to clinical judgment. Clinical judgment should always be used when interpreting the NOL index in conjunction with other available clinical and vital signs.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the PMD-200, and substantially equivalent devices of this generic type, into Class II under the generic name adjunctive pain measurement device for anesthesiology.

FDA identifies this generic type of device as:

> **Adjunctive pain measurement device for anesthesiology**. An adjunctive pain measurement device for anesthesiology is a prescription device that includes software algorithms to analyze physiological sensor data and measure response to painful stimuli in patients under general anesthesia. The device may be software-only or it may include hardware such as physiological sensors. This device type is

  intended for adjunctive use to tailor analgesic administration to a patient's actual response to painful stimuli and is not intended to independently direct decision-making.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On July 28, 2022, FDA received your De Novo requesting classification of the PMD-200. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the PMD-200 into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the PMD-200 can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	Mitigation Measures
Delayed or incorrect treatment due to erroneous device output resulting from software malfunction or algorithm error	Clinical performance testing Non-clinical performance testing Software verification, validation, and hazard analysis Labeling
Delayed or incorrect treatment due to user misinterpretation or overreliance on indicator	Usability assessment Labeling
Adverse tissue reaction	Biocompatibility Evaluation
Electric shock/electromagnetic interference related to hardware	Electrical safety testing Electromagnetic compatibility testing

In combination with the general controls of the FD&C Act, the adjunctive pain measurement device for anesthesiology is subject to the following special controls:

(1) Clinical data must be provided to validate the algorithm in support of the intended use and include the following:

(i)   Comparison of output measure(s) to a reference method to demonstrate the required accuracy and/or sensitivity and specificity of the output measure(s);

(ii)   Demonstration of the consistency of the output and representativeness of the range of data sources and data quality likely to be encountered in the intended use population and relevant use conditions in the intended use environment;

(iii)   Evaluation of the type of pain (e.g., nociceptive, somatic, visceral, neuropathic) that is within the scope of the indicated use; and

(iv)   For devices using algorithms based on machine learning, the clinical validation must be completed using a dataset that is separate from the training dataset.

(2) Software description, verification, and validation based on comprehensive hazard analysis must be performed. Software documentation must include:

(i)   Full characterization of technical parameters of the software, including any algorithm(s);

(ii)   Description of mechanisms for handling of noisy or missing data and poor signal quality under expected conditions of use;

(iii)   Specification of acceptable incoming sensor data quality control measures;

(iv)   Mitigation of impact of user error or failure of any subsystem components (signal detection and analysis, data display, and storage) on output accuracy; and

(v)   Justification for the validity of the algorithm(s) (e.g., clinical relevance of decision threshold).

(3) Non-clinical performance data must demonstrate that the device performs as intended under anticipated conditions of use. Performance testing under anticipated conditions of use must demonstrate the ability of the device software/algorithm to detect adequate input signal quality and handle noisy or missing data and poor signal quality.

(4) Usability assessment must be provided to mitigate the risk of misinterpretation of device output.

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

(6) Performance testing must demonstrate the electromagnetic compatibility (EMC) and electrical safety of any hardware components of the device.

(7) Labeling must include the following:

(i)   A summary of the clinical validation data, including demographics and other relevant characteristics of the clinical study participants (including age, gender, race or ethnicity, and patient condition), the anesthetic regimen (including types (e.g., morphine, hydromorphone, fentanyl, etc. and doses of pain medication used), a summary of results, and information on subpopulations (age, gender, race, or ethnicity) that may experience disparate performance.

(ii)   A description of what the device measures and outputs to the user.

(iii)   The type of sensor data used, including specification of compatible sensors for data acquisition.

(iv)   Warnings identifying sensor signal-acquisition factors that may impact output.

(v)   Warnings to identify and avoid specific patient conditions or concomitant medical therapies that could mask pain or negatively impact device performance leading to inaccurate measurements; and

(vi)   Recommendations for clinical interpretation of the output, including warning(s) emphasizing the adjunctive use of the output measure(s).

In addition, this is a prescription device and must comply with 21 CFR 801.109.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the adjunctive pain measurement device for anesthesiology they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C 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 FD&C Act; 21 CFR 1000-1050).

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, 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).

If you have any questions concerning the contents of the letter, please contact Neel Patel at 301-796-6274.

Sincerely,

for Malvina B. Eydelman, M.D.
    Director
    OHT1: Office of Ophthalmic, Anesthesia,
        Respiratory, ENT and Dental Devices
    Office of Product Evaluation and Quality
    Center for Devices and Radiological Health