4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 868

[Docket No. FDA-2026-N-5825]

Medical Devices; Anesthesiology Devices; Classification of the Adjunctive Pain Measurement Device for Anesthesiology

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA) is classifying the adjunctive pain measurement device for anesthesiology into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for classification of the adjunctive pain measurement device for anesthesiology. We are taking this action because we have determined that classifying the device into class II will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices, in part by reducing regulatory burdens.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The classification was applicable on February 17, 2023.

FOR FURTHER INFORMATION CONTACT: Neel Patel, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 1232, Silver Spring, MD 20993-0002, 301-796-6274, Neel.Patel@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA (the Agency or we) has classified the adjunctive pain measurement device for anesthesiology into class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness of the device. In addition, we believe this

action will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens by placing the device into a lower device class than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified into, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (21 U.S.C. 360c(f)(1)). We refer to these devices as "postamendments devices" because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate device by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through "De Novo" classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act (see also part 860, subpart D (21 CFR part 860, subpart D)). Section 207 of the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) modified the De Novo classification process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a premarket notification (510(k)) for a device that has not previously been classified. After receiving an order from FDA classifying the

device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

We believe this De Novo classification will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens. When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see section 513(f)(2)(B)(i) of the FD&C Act). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application to market a substantially equivalent device (see section 513(i) of the FD&C Act, defining "substantial equivalence"). Instead, sponsors can use the less burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

On June 4, 2021, FDA received Medasense Biometrics Ltd.'s request for De Novo classification of the PMD-200 device. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness of the device, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see

section 513(a)(1)(B) of the FD&C Act). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on February 17, 2023, FDA issued an order to the requester classifying the device into class II. In this final order, FDA is codifying the classification of the device by adding 21 CFR 868.2200.[1] We have named the generic type of device "adjunctive pain measurement device for anesthesiology," and it is identified as 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.

FDA has identified the risks to health associated with this type of device and the measures required to mitigate these risks in table 1.

Table 1.--Risks to Health and Mitigation Measures for Adjunctive Pain Measurement Devices for Anesthesiology

Identified 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; and Labeling
Delayed or incorrect treatment due to user misinterpretation or overreliance on indicator	Usability assessment; and Labeling
Adverse tissue reaction	Biocompatibility evaluation
Electric shock/electromagnetic interference related to hardware	Electrical safety testing; and Electromagnetic compatibility testing

[1] FDA notes that the "ACTION" caption for this final order is styled as "Final amendment; final order," rather than "Final order." Beginning in December 2019, this editorial change was made to indicate that the document "amends" the Code of Federal Regulations. The change was made in accordance with the Office of Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

FDA has determined that special controls, in combination with the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness of the device. For a device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this final order.

At the time of classification, adjunctive pain measurement devices for anesthesiology are for prescription use only. Prescription devices are exempt from the requirement for adequate directions for use for the layperson under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) and 21 CFR 801.5, as long as the conditions of 21 CFR 801.109 are met.

Under the FD&C Act, submission of a premarket notification under section 510(k) is required to reasonably assure the safety and effectiveness of class II devices unless FDA determines that the device type should be exempt under section 510(m) of the FD&C Act. At this time FDA has not made this determination for adjunctive pain measurement devices for anesthesiology. This device is therefore subject to premarket notification requirements under section 510(k) of the FD&C Act.

III. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not normally have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Paperwork Reduction Act of 1995

This final order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in part 860, subpart D, regarding De Novo classification have been approved under OMB control number 0910-0844; the collections of information in 21 CFR part 814, subparts A through E, regarding

premarket approval have been approved under OMB control number 0910-0231; the collections of information in part 807, subpart E, regarding premarket notification submissions have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 820 regarding quality management system regulation have been approved under OMB control number 0910-0073; and the collections of information in 21 CFR part 801 regarding labeling have been approved under OMB control number 0910-0485.

List of Subjects in 21 CFR Part 868

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 868 is amended as follows:

PART 868—ANESTHESIOLOGY DEVICES

1. The authority citation for part 868 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

2. Add § 868.2200 to subpart C to read as follows:

§ 868.2200 Adjunctive pain measurement device for anesthesiology.

(a) *Identification*. 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.

(b) *Classification*. Class II (special controls). The special controls for this device are:

(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 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, sex, race or ethnicity, and patient condition), the anesthetic regimen (including types (e.g., morphine, hydromorphone, fentanyl) and doses of pain medication used), a summary of results, and information on subpopulations (age, sex, 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.

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

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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