March 31, 2023

Masimo Corporation
Mr. Linus Park
Vice President, Regulatory
52 Discovery
Irvine, CA 91628

Re: DEN200011
Trade/Device Name: Masimo SafetyNet Opioid System
Regulation Number: 21 CFR 868.2250
Regulation Name: Monitor for opioid induced impairment of oxygenation
Regulatory Class: Class II
Product Code: QVT
Dated: February 17, 2020
Received: February 19, 2020

Dear Mr. Park:

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 Masimo SafetyNet Opioid System, both a prescription device under 21 CFR part 801.109 and an over-the-counter device under 21 CFR part 801 subpart C, with the following indications for use:

> The Masimo SafetyNet Opioid System is intended to monitor and alarm when a patient may be experiencing an opioid induced impairment of oxygenation.
>
> The Masimo SafetyNet Opioid System is indicated for the non-invasive continuous monitoring of individuals 15 years and older for the identification of when they may be experiencing a substance induced impairment of oxygenation (e.g., opioid induced respiratory depression (OIRD) caused by oral or injectable opioids) in hospital and home environments.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Masimo SafetyNet Opioid System, and substantially equivalent devices of this generic type, into Class II under the generic name monitor for opioid induced impairment of oxygenation.

FDA identifies this generic type of device as:

> **Monitor for opioid induced impairment of oxygenation.** A monitor for opioid induced impairment of oxygenation is a device that uses sensor hardware and software algorithms to detect desaturations of arterial oxygen saturation resulting from opioid overdose.

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 March 7, 2023, FDA received your De Novo requesting classification of the Masimo SafetyNet Opioid System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Masimo SafetyNet Opioid System 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 Masimo SafetyNet Opioid System 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:

Identified Risks to Health	Mitigation Measures
False negative leading to delayed treatment	Clinical performance data Non-clinical performance testing Software validation, verification, and hazard analysis Labeling
False positive based on other medical conditions or poor algorithm performance leading to unnecessary early intervention or response	Clinical performance data Non-clinical performance testing Software validation, verification, and hazard analysis Labeling
Software malfunction that causes an algorithm error	Software validation, verification, and hazard analysis
Delayed or incorrect treatment due to use-related error or overreliance on device	Usability assessment Labeling
Adverse tissue reaction	Biocompatibility evaluation
Sensor induced injury	Electrical, thermal, and mechanical safety testing
Failure to function as intended due to electromagnetic and wireless radio frequency interference	Electromagnetic compatibility testing Wireless coexistence testing

In combination with the general controls of the FD&C Act, the monitor for opioid induced impairment of oxygenation is subject to the following special controls:

(1) Clinical performance data under anticipated conditions of use must demonstrate that the device performs as intended and include the following:

(i) Comparison to a clinically relevant reference method to demonstrate and support the accuracy and level of sensitivity and specificity for detection of opioid induced impairment of oxygenation;
(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) Performance reported in clinically significant and distinct subpopulations and intended use environments;
(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; and
(v) Simulated use testing of hardware and sensors to characterize accuracy and precision across the intended use population.

(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) Specification of acceptable incoming sensor data quality control measures; and
(iii) Justification for the validity of the algorithm(s) (e.g., clinical relevance/importance of decision threshold).

(3) Non-clinical performance data must demonstrate that the device performs as intended under anticipated conditions of use. Testing must include:
(i) Performance testing of sensor hardware to characterize sensor accuracy and precision; and
(ii) Compatibility testing of sensors with other hardware and software components of the device.

(4) Usability assessment must be provided to demonstrate that intended device users can safely and correctly use the device.

(5) All components of the device that contact the skin must be demonstrated to be biocompatible.

(6) Performance testing must demonstrate the electromagnetic compatibility (EMC), wireless coexistence, electrical safety, thermal safety, and mechanical safety of any hardware components and sensors of the device.

(7) Labeling must include the following:

(i) A summary of the clinical validation data, including relevant characteristics of the included subpopulations and use environments in the clinical study, and performance metrics, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each of the subpopulations, use environments, and opioid types;

(ii) Principles of sensor operation, including warnings for how to avoid interfering with sensor readings;
(iii) Information for preventing an overdose, recognizing signs of an overdose, and treating an overdose;
(iv) Warnings identifying that the device is not designed to differentiate between the target condition (e.g., opioid-induced respiratory depression) and other conditions that may cause a false reading (e.g., obstructive sleep apnea);
(v) Warnings against overreliance on the device; and
(vi) A warning regarding the need for supervised use with awareness of effective countermeasures (e.g., naloxone) in case of an overdose.

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 monitor for opioid induced impairment of oxygenation 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,

Bradley S. Cunningham -S

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