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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 862

[Docket No. FDA–2021–N–1343]

Medical Devices; Clinical Chemistry and Clinical Toxicology Devices; Classification of the Integrated Continuous Glucose Monitoring System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the integrated continuous glucose monitoring system 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 the integrated continuous glucose monitoring system's classification. We are taking this action because we have determined that classifying the device into class II (special controls) 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.

DATES: This order is effective February 18, 2022. The classification was applicable on March 27, 2018.

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SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the integrated continuous glucose monitoring system as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. In addition, we believe this action will enhance patients' access to beneficial innovation, in part 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 as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 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. 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 application 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 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.

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 December 8, 2017, FDA received Dexcom, Inc.'s request for De Novo classification of the Dexcom G6 Continuous Glucose Monitoring System. 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, 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 21 U.S.C. 360c(a)(1)(B)). 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 March 27, 2018, 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 862.1355.[1] We have named the generic type of device ''integrated continuous glucose monitoring system (iCGM),'' and it is intended to automatically measure glucose in bodily fluids continuously or frequently for a specified period of time. iCGM systems are designed to reliably and securely transmit glucose measurement data to digitally connected devices, including automated insulin dosing systems, and are intended to be used alone or in conjunction with these digitally connected medical devices for the purpose of managing a disease or condition related to glycemic control.

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

TABLE 1—INTEGRATED CONTINUOUS GLUCOSE MONITORING SYSTEM RISKS AND MITIGATION MEASURES

Identified risks	Mitigation measures
Clinical action based on falsely high or falsely low inaccurate glucose values or inaccurate alerts may lead to inappropriate treatment decisions.	General Controls and special controls (1) (21 CFR 862.1355(b)(1)), (2) (21 CFR 862.1355(b)(2)), (3) (21 CFR 862.1355(b)(3)), (4) (21 CFR 862.1355(b)(4)), (5) (21 CFR 862.1355(b)(5)), (6) (21 CFR 862.1355(b)(6)), and (7) (21 CFR 862.1355(b)(7)).
Clinical action in pediatric patients based on falsely high or falsely low inaccurate values or inaccurate alerts due to poorer or different performance in pediatric populations.	General Controls and special controls (1) (21 CFR 862.1355(b)(1)), (2) (21 CFR 862.1355(b)(2)), (3) (21 CFR 862.1355(b)(3)), (4) (21 CFR 862.1355(b)(4)), (5) (21 CFR 862.1355(b)(5)), (6) (21 CFR 862.1355(b)(6)), and (7) (21 CFR 862.1355(b)(7)).
The inability to make appropriate treatment decisions when glucose values are unavailable due to sensor signal dropout or loss of communication with digitally connected devices.	General Controls and special controls (1)(vii) (21 CFR 862.1355(b)(1)(vii)), (2) (21 CFR 862.1355(b)(2)), (3) (21 CFR 862.1355(b)(3)), (6) (21 CFR 862.1355(b)(6)), and (7) (21 CFR 862.1355(b)(7)).
Patient harm due to insecure transmission of data	General Controls and special control (2) (21 CFR 862.1355(b)(2)).
Use of an iCGM as part of another digitally connected medical device system, such as an automated insulin dosing (AID) system, when the iCGM has inadequate analytical or clinical performance to support the intended use of the digitally connected device.	General Controls and special controls (2) (21 CFR 862.1355(b)(2)), (6) (21 CFR 862.1355(b)(6)), and (7) (21 CFR 862.1355(b)(7)).

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. In order 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 order. This device is 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 individually or cumulatively 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 the guidance document ''De Novo Classification Process (Evaluation of Automatic Class III Designation)'' 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 systems regulations, have been approved under OMB control number 0910–0073; and the collections of information in 21 CFR parts 801 and 809, regarding labeling, have been approved under OMB control number 0910–0485.

List of Subjects in 21 CFR Part 862

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 862 is amended as follows:

PART 862—CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

■ 1. The authority citation for part 862 continues to read as follows:

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

■ 2. Add § 862.1355 to subpart B to read as follows:

§ 862.1355 Integrated continuous glucose monitoring system.

(a) *Identification.* An integrated continuous glucose monitoring system (iCGM) is intended to automatically measure glucose in bodily fluids continuously or frequently for a specified period of time. iCGM systems are designed to reliably and securely transmit glucose measurement data to digitally connected devices, including automated insulin dosing systems, and are intended to be used alone or in conjunction with these digitally connected medical devices for the purpose of managing a disease or condition related to glycemic control.

[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.

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

(1) Design verification and validation must include the following:

(i) Robust clinical data demonstrating the accuracy of the device in the intended use population.

(ii) The clinical data must include a comparison between iCGM values and blood glucose values in specimens collected in parallel that are measured on an FDA-accepted laboratory-based glucose measurement method that is precise and accurate, and that is traceable to a higher order (*e.g.,* an internationally recognized reference material and/or method).

(iii) The clinical data must be obtained from a clinical study designed to fully represent the performance of the device throughout the intended use population and throughout the measuring range of the device.

(iv) Clinical study results must demonstrate consistent analytical and clinical performance throughout the sensor wear period.

(v) Clinical study results in the adult population must meet the following performance requirements:

(A) For all iCGM measurements less than 70 milligrams/deciliter (mg/dL), the percentage of iCGM measurements within ±15 mg/dL of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 85 percent.

(B) For all iCGM measurements from 70 mg/dL to 180 mg/dL, the percentage of iCGM measurements within ±15 percent of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 70 percent.

(C) For all iCGM measurements greater than 180 mg/dL, the percentage of iCGM measurements within ±15 percent of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 80 percent.

(D) For all iCGM measurements less than 70 mg/dL, the percentage of iCGM measurements within ±40 mg/dL of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 98 percent.

(E) For all iCGM measurements from 70 mg/dL to 180 mg/dL, the percentage of iCGM measurements within ±40 percent of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 99 percent.

(F) For all iCGM measurements greater than180 mg/dL, the percentage of iCGM measurements within ±40 percent of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 99 percent.

(G) Throughout the device measuring range, the percentage of iCGM measurements within ±20 percent of the corresponding blood glucose value must be calculated, and the lower one-sided 95 percent confidence bound must exceed 87 percent.

(H) When iCGM values are less than 70 mg/dL, no corresponding blood glucose value shall read above 180 mg/dL.

(I) When iCGM values are greater than 180 mg/dL, no corresponding blood glucose value shall read less than 70 mg/dL.

(J) There shall be no more than 1 percent of iCGM measurements that indicate a positive glucose rate of change greater than 1 mg/dL per minute (/min) when the corresponding true negative glucose rate of change is less than -2 mg/dL/min as determined by the corresponding blood glucose measurements.

(K) There shall be no more than 1 percent of iCGM measurements that indicate a negative glucose rate of change less than -1 mg/dL/min when the corresponding true positive glucose rate of change is greater than 2 mg/dL/min as determined by the corresponding blood glucose measurements.

(vi) Data demonstrating similar accuracy and rate of change performance of the iCGM in the pediatric population as compared to that in the adult population, or alternatively a clinical and/or technical justification for why pediatric data are not needed, must be provided and determined by FDA to be acceptable and appropriate.

(vii) Data must demonstrate that throughout the claimed sensor life, the device does not allow clinically significant gaps in sensor data availability that would prevent any digitally connected devices from achieving their intended use.

(2) Design verification and validation must include a detailed strategy to ensure secure and reliable means of iCGM data transmission to provide real-time glucose readings at clinically meaningful time intervals to devices intended to receive the iCGM glucose data.

(3) Design verification and validation must include adequate controls established during manufacturing and at product release to ensure the released product meets the performance specifications as defined in paragraphs (b)(1) and (b)(2) of this section.

(4) The device must demonstrate clinically acceptable performance in the presence of clinically relevant levels of potential interfering substances that are reasonably present in the intended use population, including but not limited to endogenous substances and metabolites, foods, dietary supplements, and medications.

(5) The device must include appropriate measures to ensure that disposable sensors cannot be used beyond its claimed sensor wear period.

(6) Design verification and validation must include results obtained through a usability study that demonstrates that the intended user can use the device safely and obtain the expected glucose measurement accuracy.

(7) The labeling required under § 809.10(b) of this chapter must include a separate description of the following sensor performance data observed in the clinical study performed in conformance with paragraph (b)(1) of this section for each intended use population, in addition to separate sensor performance data for each different iCGM insertion or use sites (*e.g.,* abdomen, arm, buttock):

(i) A description of the accuracy in the following blood glucose concentration ranges: less than 54 mg/dL, 54 mg/dL to less than 70 mg/dL, 70 to 180 mg/dL, greater than 180 to 250 mg/dL, and greater than 250 mg/dL.

(ii) A description of the accuracy of positive and negative rate of change data.

(iii) A description of the frequency and duration of gaps in sensor data.

(iv) A description of the true, false, missed, and correct alert rates and a description of the available glucose concentration alert settings, if applicable.

(v) A description of the observed duration of iCGM life for the device.

Dated: February 11, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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