4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 876

[Docket No. FDA-2026-N-6536]

Medical Devices; Gastroenterology-Urology Devices; Classification of the Ingestible Gastrointestinal Blood Detection Capsule

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA) is classifying the ingestible gastrointestinal blood detection capsule 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 ingestible gastrointestinal blood detection capsule. 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 24, 2023.

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SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA (the Agency or we) has classified the ingestible gastrointestinal blood detection capsule 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 September 29, 2022, FDA received EnteraSense Ltd.'s request for De Novo classification of the Pill Sense 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 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 24, 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 876.1390.[1] We have named the generic type of device "ingestible gastrointestinal blood detection capsule," and it is identified as a prescription device that uses spectrophotometry (light absorption technology) to detect the presence or absence of blood in the gastrointestinal tract.

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 Ingestible Gastrointestinal Blood Detection Capsule

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Failure to accurately detect blood leading to misdiagnosis or delayed diagnosis	Clinical performance testing; Non-clinical performance testing; Software validation, verification, and hazard analysis; and Labeling
Infection	Non-clinical performance testing; Shelf life and package integrity testing; and Labeling
Device failure/malfunction leading to injury	Electrical, thermal, and mechanical safety testing; Software validation, verification, and hazard analysis; Usability testing; Non-clinical performance testing; Shelf life testing; and Labeling
Device failure to function as intended due to interference with other devices (e.g., interference with data acquisition)	Electromagnetic compatibility testing; and Labeling

[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.

Failure to excrete the capsule leading to injury	Clinical performance testing; and Labeling

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, ingestible gastrointestinal blood detection capsules 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 ingestible gastrointestinal blood detection capsules. 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 876

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 876 is amended as follows:

PART 876--GASTROENTEROLOGY-UROLOGY DEVICES

1. The authority citation for part 876 continues to read as follows:

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

2. Add § 876.1390 to subpart B to read as follows:

§ 876.1390 Ingestible gastrointestinal blood detection capsule.

(a) *Identification*. An ingestible gastrointestinal blood detection capsule device is a prescription device that uses spectrophotometry (light absorption technology) to detect the presence or absence of blood in the gastrointestinal tract.

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

(1) Clinical performance testing must demonstrate the device performs as intended under anticipated conditions of use. Testing must evaluate:

(i) Detection of presence or absence of blood when compared to endoscopic procedures used to detect upper gastrointestinal bleeding;

(ii) Capsule excretion and recovery; and

(iii) All adverse events.

(2) Non-clinical performance testing must demonstrate the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:

(i) Dimensional testing must verify device dimensions;

(ii) Performance testing must verify functional aspects of the device design;

(iii) Battery life testing must be performed to demonstrate the capsule's operating time is not constrained by the battery capacity;

(iv) Leak testing must verify device integrity under worst-case clinical conditions;

(v) Bite testing must demonstrate that the device can withstand bite forces;

(vi) pH resistance testing must evaluate integrity of the capsule when exposed to a physiological relevant range of pH values;

(vii) Control and monitoring of capsule bioburden must demonstrate the device does not pose an infection risk; and

(viii) Blood detection testing must demonstrate that the device can detect different forms of blood seen under anticipated conditions of use.

(3) Software validation, verification, and hazard analysis must be performed.

(4) Electrical safety, thermal safety, mechanical safety, and electromagnetic compatibility testing must be performed.

(5) Usability assessment must demonstrate that the intended user(s) can safely and correctly use the device.

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

(7) Performance testing must support the shelf life of the device by demonstrating continued package integrity and device functionality over the identified shelf life.

(8) Physician labeling must include:

(i) A detailed summary of the clinical testing pertinent to use of the device, including information on effectiveness and device- and procedure-related complications;

(ii) Warning that the device is not a standalone diagnostic device and does not replace clinical decision making; and

(iii) A shelf life.

(9) Patient labeling must include:

(i) An explanation of the device and the mechanism of operation;

(ii) The patient preparation procedure;

(iii) A brief summary of the clinical study; and

(iv) A summary of the device- and procedure-related complications pertinent to use of the device.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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