February 24, 2023

EnteraSense Ltd.
% Annette Fagnant
Regulatory Consultant
MedDRA Assistance, Inc.
55 Peaceful Way
Tiverton, RI 02878

Re: DEN220065
Trade/Device Name: Pill Sense System
Regulation Number: 21 CFR 876.1390
Regulation Name: Ingestible gastrointestinal blood detection capsule
Regulatory Class: Class II
Product Code: QUD
Dated: September 28, 2022
Received: September 29, 2022

Dear Annette Fagnant:

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 Pill Sense System, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> The PillSense System is a prescription only device consisting of a reusable receiver and single-use ingestible capsule, intended to be used for the detection of blood in the upper gastrointestinal tract in hemodynamically stable adults suspected of having upper gastrointestinal bleeding (UGIB).
>
> PillSense is not a standalone diagnostic device, but an adjunct for clinical decision making. A negative or normal result obtained by PillSense System does not exclude presence of pathology, if symptoms persist, further evaluation should be performed.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Pill Sense System, and substantially equivalent devices of this generic type, into Class II under the generic name ingestible gastrointestinal blood detection capsule.

FDA identifies this generic type of device as:

> **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.

Section 513(f)(2) of the Federal 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 September 29, 2022, FDA received your De Novo requesting classification of the Pill Sense System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Pill Sense 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 Pill Sense 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**
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 Labeling
Infection	Non-clinical performance testing Shelf life and package integrity testing 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 Labeling
Device failure to function as intended due to interference with other devices	Electromagnetic compatibility testing Labeling

Identified Risks to Health	Mitigation Measures
(e.g., interference with data acquisition)	
Failure to excrete the capsule leading to injury	Clinical performance testing Labeling

In combination with the general controls of the FD&C Act, the ingestible gastrointestinal blood detection capsule is subject to the following special controls:

(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 (EMC) testing must be performed.

(5) Usability assessment must demonstrate that the intended users(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.

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 ingestible gastrointestinal blood detection capsule that 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 Sivakami Venkatachalam at 301-796-9103.

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
OHT3: Office of GastroRenal, ObGyn,
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Office of Product Evaluation and Quality
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