combinations and storage/use conditions that will be indicated, including specimen transport, as appropriate.

(2) The intended use for the labeling required under § 809.10(a)(4) of this chapter and for the labeling required under § 809.10(b)(5)(ii) of this chapter, as applicable, must include:

(i) The clinical hematopoietic malignancy for which the assay was designed and validated (*e.g.,* multiple myeloma or B-cell acute lymphoblastic leukemia);

(ii) Specimen type (*e.g.,* bone marrow);

(iii) The specific DNA regions that are being identified and quantified (*e.g.,* rearranged IgH (VDJ), IgH (DJ), IgK, and IgL receptor gene sequences); and

(iv) A statement that the results are indicated to be interpreted by qualified healthcare professionals in accordance with professional guidelines for clinical decision-making in conjunction with other clinicopathological features.

(3) The labeling required under § 809.10(b) of this chapter must include information that demonstrates the performance characteristics of the test, including a detailed summary of the performance studies conducted and their results, as described in paragraphs (b)(1)(iv)(A) through (I) of this section.

(4) The device output, including any test report, must include the estimated minimal residual disease (MRD) frequency and an appropriate range of the uncertainty of that frequency based on the amount of DNA that was evaluated by the test and the number of specific nucleic acid sequences that were detected (*e.g.,* ''MRD = 1.2×10^{-5} [Range = 0.8×10^{-6} to 2.0×10^{-5}]'').

Dated: May 5, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–08143 Filed 5–8–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2025–N–0781]

Medical Devices; Immunology and Microbiology Devices; Classification of the Device To Detect and Measure Non-Microbial Analytes To Aid in the Detection and Identification of Localized Human Infections

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is classifying the device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections 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 device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections' 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, in part by reducing regulatory burdens.

DATES: This order is effective May 9, 2025. The classification was applicable on May 23, 2019.

FOR FURTHER INFORMATION CONTACT: Dina Jerebitski, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3574, Silver Spring, MD 20993–0002, 301–796–2411, *Dina.Jerebitski@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections 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 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 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 (see 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 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.

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 29, 2018, FDA received CD Diagnostics Inc.'s request for De Novo classification of the Synovasure Alpha Defensin Lateral Flow Test Kit, Synovasure Alpha Defensin Lateral Flow Test Kit (5 Test), Synovasure Alpha Defensin Lateral Flow Test Kit (10 Test), Synovasure Alpha Defensin Lateral Flow Test Kit (30 Test), and the Synovasure Alpha Defensin Control Kit. 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 May 23, 2019, 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 866.3230.[1] We have named the generic type of device ''Device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections,'' and it is identified as an in vitro diagnostic device intended for the detection and qualitative measurement, quantitative measurement, or both of one or more non-microbial analytes in human clinical specimens to aid in the assessment, identification, or both of a localized microbial infection when used in conjunction with clinical signs and symptoms and other clinical and laboratory findings.

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—DEVICE TO DETECT AND MEASURE NON-MICROBIAL ANALYTES TO AID IN THE DETECTION AND IDENTIFICATION OF LOCALIZED HUMAN INFECTIONS RISKS AND MITIGATION MEASURES

Identified risks to health	Mitigation measures
Risk of false test results	Certain device descriptions, performance characteristics, results interpretation information, limitations, and study details in labeling; Certain device description information, demographic analysis, validation procedures, risk mitigation strategies and end user trainings, and studies; and Collection device specification.
Failure to interpret test results correctly.	Certain device descriptions, performance characteristics, results interpretation information, limitations, and study details in labeling; and Certain demographic analysis, validation procedures, risk mitigation strategies and end user trainings, and studies.
Failure to operate the device correctly.	Certain device descriptions, performance characteristics, results interpretation information, limitations, and study details in labeling; Certain demographic analysis, validation procedures, risk mitigation strategies and end user trainings, and studies; and Collection device specification.

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. 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 part 860, subpart D, regarding De Novo

[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 the 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.

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 the Quality System Regulation, 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 866

Biologics, Laboratories, 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 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for part 866 continues to read as follows:

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

■ 2. Add § 866.3230 to subpart D to read as follows:

§ 866.3230 Device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections.

(a) *Identification.* A device to detect and measure non-microbial analytes to aid in the detection and identification of localized human infections is identified as an in vitro diagnostic device intended for the detection and qualitative measurement, quantitative measurement, or both of one or more non-microbial analytes in human clinical specimens to aid in the assessment, identification, or both of a localized microbial infection when used in conjunction with clinical signs and symptoms and other clinical and laboratory findings.

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

(1) Any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of human specimens; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.

(2) The labeling required under § 809.10(b) of this chapter must include:

(i) An intended use with a detailed description of what the device detects and measures, the type of results provided to the user, the sample type, whether the measure is qualitative and/or quantitative, the clinical indications for the test use, and the specific population(s) for which the device is intended.

(ii) A detailed description of the performance characteristics of the device for all intended specimen types from the analytical and clinical studies (as applicable) required under paragraphs (b)(3)(ii) and (iii) of this section.

(iii) A detailed explanation of the interpretation of results, including acceptance criteria for evaluating the validity of individual runs (*e.g.,* assessment of internal and/or external quality controls, as applicable).

(iv) The following limiting statements:

(A) A statement that a negative test result does not preclude the possibility of infection;

(B) A statement that the test results should be interpreted in conjunction with other clinical and laboratory data available to the clinician;

(C) A statement that consistent device performance is dependent on adequate specimen collection, transport, storage, and processing. Failure to observe proper procedures in any one of these steps can lead to incorrect results; and

(D) A statement that details any limitations associated with the samples, as appropriate (*e.g.,* collected on the day of admission to the intensive care unit).

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

(i) A detailed device description, including as appropriate, all device parts; control elements incorporated into the test procedure; instrument requirements; reagents required but not provided; and the principle of device operation and test methodology, including all preanalytical methods for the processing of specimens and the methodology from obtaining a sample to the result; design of primer/probe sequences; rationale for target analyte selection; and computational path from collected raw data to reported result (*e.g.,* how collected raw signals are converted into a reported result).

(ii) Detailed documentation of analytical studies including analytical sensitivity (Limit of Detection, Limit of Quantitation, and Limit of Blank), inclusivity, cross-reactivity, microbial interference, interfering substances, competitive inhibition, carryover/cross-contamination, specimen stability, within-lab precision, reproducibility, and linearity, as applicable.

(iii) Detailed documentation and results either from a clinical study, that includes prospective (sequentially collected) samples for each intended specimen type that are representative of the intended use populations and, when determined to be acceptable by FDA, additional characterized clinical samples; or, when determined to be acceptable by FDA, an equivalent sample set. The clinical study must compare the device performance to results obtained from an FDA-accepted reference method and/or FDA-accepted comparator method, as appropriate. Documentation from the clinical studies must include the clinical study protocol (*e.g.,* the predefined statistical analysis plan), clinical study report, testing results, and results of all statistical analyses.

(iv) An evaluation of the level of the non-microbial analyte in asymptomatic patients with demographic characteristics (*e.g.,* age, racial, ethnic, and sex distribution) similar to the intended use population of the device.

(v) Documentation of an appropriate end user device training program that will be offered as part of efforts to mitigate the risks of false results, failure to operate the device correctly, and failure to interpret test results correctly.

(vi) An appropriate risk mitigation strategy to ensure that the device does not prevent any other device(s) with which it is indicated for use, including incorporated device(s), from achieving their intended use (*e.g.,* safety and effectiveness of the functions of the indicated device(s) remain unaffected).

(vii) A detailed description of the impact of any software, including software applications and hardware-based devices that incorporate software, on the device's functions.

Dated: May 5, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–08144 Filed 5–8–25; 8:45 am]

BILLING CODE 4164–01–P