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 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, subpart 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 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 § 866.3367 to subpart D to read as follows:

§ 866.3367 Device to detect and identify microbial nucleic acids by FISH in clinical specimens.

(a) *Identification.* A device to detect and identify microbial nucleic acids by fluorescence in situ hybridization (FISH) in clinical specimens is an in vitro diagnostic device intended for the detection and identification of microbial pathogens in specimens collected from patients with signs and symptoms of infection. The device is intended to aid in the diagnosis of human disease in conjunction with clinical signs and symptoms and other laboratory findings.

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

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

(i) Detailed device description documentation, including the device components, instrument requirements, ancillary reagents required but not provided, and a detailed explanation of the methodology, including all pre-analytical methods for processing of specimens, probe sequences, and rationale for probe sequence selection;

(ii) Detailed description of the fluorophores, signal source, detection mechanism, and method of result interpretation;

(iii) Detailed documentation from the following analytical studies: analytical sensitivity (Limit of Detection), inclusivity, reproducibility, interference, cross reactivity, and specimen stability; and

(iv) Detailed documentation from a clinical study that includes prospective (sequential) samples. The study, performed on a study population consistent with the intended use population, must compare the device performance to results obtained from appropriate and well-accepted comparator methods.

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

(i) A statement that the device is intended to be used in conjunction with clinical history, signs, symptoms, and the results of other diagnostic testing;

(ii) A detailed explanation of the interpretation of results and acceptance criteria for any quality control testing; and

(iii) A limitation that negative results do not preclude the possibility of infection.

Dated: May 5, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–08150 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–0708]

Medical Devices; Immunology and Microbiology Devices; Classification of the DNA-Based Test To Measure Minimal Residual Disease in Hematological Malignancies

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

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the DNA-based test to measure minimal residual disease in hematological malignancies 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 DNA-based test to measure minimal residual disease in hematological malignancies 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 September 28, 2018.

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 DNA-based test to measure minimal residual disease in hematological malignancies 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 September 29, 2017, FDA received Adaptive Biotechnologies Corporation's request for De Novo classification of the clonoSEQ Assay. 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 September 28, 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 866.6100.[1] We have named the generic type of device ''DNA-based test to measure minimal residual disease in hematological malignancies,'' and it is identified as a prescription in vitro diagnostic device that identifies and quantifies specific nucleic acid sequences within human tissues to estimate the percentage of cells that harbor the specific sequence(s). The test is intended to be used as an aid to measure minimal residual disease to assess the change in burden of disease during monitoring of treatment. The test is indicated for use by qualified healthcare professionals in accordance with professional guidelines for clinical decision-making, in conjunction with other clinicopathological features.

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—DNA-BASED TEST TO MEASURE MINIMAL RESIDUAL DISEASE IN HEMATOLOGICAL MALIGNANCIES RISKS AND MITIGATION MEASURES

Identified risks to health	Mitigation measures
Incorrect test results	General controls and special controls (1) (21 CFR 866.6100(b)(1)), (2) (21 CFR 866.6100(b)(2)), and (3) (21 CFR 866.6100(b)(3)).
Incorrect interpretation of test results.	General controls and special controls (1) (21 CFR 866.6100(b)(1)), (2) (21 CFR 866.6100(b)(2)), (3) (21 CFR 866.6100(b)(3)), and (4) (21 CFR 866.6100(b)(4)).

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

[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.

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 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, subpart 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 § 866.6100 to subpart G to read as follows:

§ 866.6100 DNA-based test to measure minimal residual disease in hematological malignancies.

(a) *Identification.* A DNA-based test to measure minimal residual disease in hematological malignancies is a prescription in vitro diagnostic device that identifies and quantifies specific nucleic acid sequences within human tissues to estimate the percentage of cells that harbor the specific sequence(s). The test is intended to be used as an aid to measure minimal residual disease to assess the change in burden of disease during monitoring of treatment. The test is indicated for use by qualified healthcare professionals in accordance with professional guidelines for clinical decision-making, in conjunction with other clinicopathological features.

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

(1) Design verification and validation must include:

(i) A detailed description of the device, including:

(A) A detailed description of all test components, reagents, instrumentation, and software, including software applications and any hardware-based devices that incorporate software.

(B) A detailed description of all genomic regions that are detected and quantified by the assay.

(C) A detailed description of the methodology and protocols for each step of the test, including description of the quality metrics, thresholds, and filters at each step of the test that are implemented for final result reporting and a description of the metrics for run-failures, specimen-failures, and invalids, as appropriate.

(D) Detailed specifications and procedures for sample collection, processing, and storage.

(E) A description of the internal and external controls that are recommended or provided. The description must identify those control elements that are incorporated into the testing procedure. If appropriate, this description must include a description of the controls and control procedures used during the sequencing and data analysis.

(ii) Identification of risk mitigation elements used by the device, including a detailed description of all additional procedures, methods, and practices incorporated into the instructions for use that mitigate risks associated with use of the device.

(iii) As part of the risk management activities, an appropriate end user device training program must be offered as an effort to mitigate the risk of failure from user error, as appropriate.

(iv) Description of analytical and clinical studies, including:

(A) Device performance data that demonstrates the ability to measure minimal residual disease in the claimed specimen type(s) from patients that are representative of the intended use population. Data can be obtained via:

(*1*) A method comparison study comparing the device to a predicate device with clinical data for the specified hematological neoplastic indication using the specified specimen type(s); or

(*2*) A clinical study demonstrating clinical validity using well characterized clinical specimens from patients with known clinical outcomes using a study design deemed acceptable by FDA.

(B) Device precision (repeatability and reproducibility) data using clinical samples covering the range of minimal residual disease frequencies reported by the test and covering the stated range of DNA inputs that are indicated as allowable for use with the test. Results shall be reported as the standard deviation and/or percentage coefficient of variation with the 95 percent confidence interval for each level tested. The study must evaluate all sources of variability, including, as appropriate, between-site and between operator (minimum of three sites of which two must be external with a minimum of two operators per site), between-day (minimum of 3 days), between-run, within-run, between-lot (minimum of three lots), between instrument (minimum of three instruments), and total variation.

(C) Device linearity data generated from samples covering the device measuring range using a dilution panel created from clinical samples.

(D) Device accuracy by comparison to flow cytometry across the measuring interval or to the predicate method across the measuring interval.

(E) Device analytic sensitivity data, including limit of blank, limit of detection, and limit of quantitation, using a dilution panel created from clinical samples.

(F) Analytical specificity data, including interference and cross-contamination, and index cross-contamination, as appropriate.

(G) Validation of pre-analytical methods, including DNA extraction methods and cell enrichment methods, as appropriate.

(H) Device stability data, including real-time stability of reagents under various storage times and temperatures.

(I) Specimen and prepared sample stability data established for each specimen matrix in the anticoagulant

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