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 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 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 § 862.3460 to subpart D to read as follows:

§ 862.3460 Plazomicin test system.

(a) *Identification.* A plazomicin test system is a device intended to measure plazomicin in human specimens. Measurements obtained by this device are used in monitoring levels of plazomicin to ensure appropriate therapy in patients with complicated urinary tract infection.

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

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

(i) Precision study data that demonstrates clinically appropriate precision of the plazomicin test system. Precision studies must include a minimum of three samples containing different concentrations of plazomicin, including near medical decision points throughout the expected therapeutic range of plazomicin. Samples near the medical decision points must be clinical specimens collected from patients taking plazomicin.

(ii) Method comparison data that demonstrates clinically appropriate accuracy of the plazomicin test system, as determined by FDA. Method comparison data must be collected at a minimum of three laboratory sites.

(iii) Data from studies appropriate to demonstrate that the device is free from clinically significant interference from co-administered medications that are used in patients with complicated urinary tract infection, as determined by FDA.

(2) The device's labeling required under § 809.10 of this chapter must include a warning statement that explains: ''This assay should only be used in conjunction with information available from clinical evaluations and other diagnostic procedures.''

Dated: May 22, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–09638 Filed 5–28–25; 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–1183]

Medical Devices; Immunology and Microbiology Devices; Classification of the Inherited Nucleotide Repeat Disorder Deoxyribonucleic Acid Test

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the inherited nucleotide repeat disorder DNA test 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 inherited nucleotide repeat disorder DNA test'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, in part by reducing regulatory burdens.

DATES: This order is effective May 29, 2025. The classification was applicable on February 21, 2020.

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 inherited nucleotide repeat disorder DNA test 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 April 18, 2019, FDA received Asuragen, Inc.'s request for De Novo classification of the AmplideX Fragile X Dx & Carrier Screen 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 February 21, 2020, 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 866.5970.[1] We have named the generic type of device inherited nucleotide repeat disorder DNA test, and it is identified as a prescription in vitro diagnostic device that is intended to detect and identify the number of nucleotide repeats in a gene using genomic DNA isolated from post-natal patient specimens. It is solely intended as an aid for carrier testing and as an aid for the diagnosis of inherited nucleotide repeat-associated disorders. Assay results are solely intended to be used in conjunction with other clinical and diagnostic findings. These tests do not include those indicated for use for fetal diagnostic testing or newborn screening.

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—INHERITED NUCLEOTIDE REPEAT DISORDER DNA TEST RISKS AND MITIGATION MEASURES

Identified risks to health	Mitigation measures
Incorrect test results	Certain design verification and validation, and Certain labeling information.
Incorrect interpretation of test results	Certain design verification and validation, and Certain labeling information.

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 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 system regulation, have been approved under OMB control number 0910–0073; and the collections of information in 21 CFR

[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.

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, 360l, 371.

■ 2. Add § 866.5970 to subpart F to read as follows:

§ 866.5970 Inherited nucleotide repeat disorder DNA test.

(a) *Identification.* An inherited nucleotide repeat disorder DNA test is a prescription in vitro diagnostic device that is intended to detect and identify the number of nucleotide repeats in a gene using genomic DNA isolated from post-natal patient specimens. It is solely intended as an aid for carrier testing and as an aid for the diagnosis of inherited nucleotide repeat-associated disorders. Assay results are solely intended to be used in conjunction with other clinical and diagnostic findings. These tests do not include those indicated for use for fetal diagnostic testing or newborn screening.

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

(1) The intended use on the device's label required under § 809.10(a)(2) of this chapter and device's labeling required under § 809.10(b)(2) of this chapter must include a statement that assay results are solely intended to be used in conjunction with other clinical and diagnostic findings, consistent with professional standards of practice, and that reflex testing, clinical genetic evaluation, and genetic counseling should be offered as appropriate.

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

(i) A warning that mosaicism detected in one tissue may not reflect mosaicism in other tissues and that the significance of mosaicism should be interpreted with caution in conjunction with other laboratory and clinical information (*e.g.,* sex of patient, diagnostic testing or carrier screening, patient symptoms) and should include appropriate genetic counseling.

(ii) A prominent statement that this test is not indicated for use for fetal diagnostic testing, newborn screening or for stand-alone diagnostic purposes.

(iii) Information that addresses how to interpret different result outputs specific to the technology, such as (peaks) in the electropherograms.

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

(i) Appropriate design features and control elements incorporated into the testing procedure that mitigate the risk of incorrect clinical results. These include controls as determined acceptable by FDA that:

(A) Enable the user to determine when the amplification may yield incorrect results,

(B) Enable the user to determine when cross contamination may have occurred;

(C) Software risk control measures that address device system hazards;

(D) Provide software traceability that ensures all hazards are adequately controlled and that all controls have been validated in the final device design; and

(E) Ensure the instructions for use and test reports appropriately inform the user about the limitations of the assay.

(ii) Validated and acceptable, as determined by FDA, criteria for test result interpretation and reporting, including result outputs.

(iii) Acceptable, as determined by FDA, evidence demonstrating the clinical validity of the device which supports each indicated diagnostic use, including for each genotype and associated phenotype used in providing a clinical determination for the target population.

(iv) Evidence demonstrating acceptable, as determined by FDA, analytical device performance. Patient specimens must represent the full spectrum of expected clinical results and be obtained through unbiased collection. Specimens must be representative of all categories of results and across the range of repeat sizes (*e.g.,* categories and repeat sizes for Fragile X syndrome are: normal 1–44 repeats; intermediate 45–54 repeats; premutation 55–200 repeats, full mutation greater than 200 repeats), across a range of allelic combinations, be near decision points, and be from both male and female subjects. The number of specimens tested must be sufficient to obtain unbiased estimates of device performance. Analytical validation must include data demonstrating acceptable, as determined by FDA:

(A) Agreement with a comparator method(s) determined to be acceptable by FDA. This evidence must demonstrate the accuracy for detecting the size of the nucleotide repeats and the diagnostic categorical calls in DNA in the indicated specimen type(s) from patients that are representative of the intended use population. Accuracy must be assessed for both diagnostic and carrier subsets independently.

(B) Device precision including repeatability and reproducibility, using clinical samples. The study must evaluate all possible sources of variability including, as appropriate, between-site and between operator at a minimum of three sites of which two must be external with a minimum of two operators per site, between-day on a minimum of 3 non-consecutive days, between-run, within-run, between-lot in a minimum of three lots, and between instrument on a minimum of three instruments. Precision must be demonstrated per specimen and determine for both categorical call and by the size of the repeat (*i.e.,* the percentage of replicates for which the allele fell within the target precision size range). Precision data must be calculated and presented with and without results determined to be invalid.

(C) Device performance at the limit of detection of each allele across the range of sizes and as a function of the indicated DNA input for the assay.

(D) Specificity of the reagents for their targets, absence of cross-reactivity, evaluation of sources of interference relevant to the specimen type, and a demonstration of the absence of cross contamination.

(E) Performance of the pre-analytical methods, including DNA extraction methods.

(F) Performance of the device across the range of indicated DNA input concentrations for the assay.

(G) Specimen stability throughout indicated specimen storage ranges, including under expected storage and transport conditions.

(v) Robust evidence demonstrating that the number and frequency of incorrect results due to mosaicism are clinically acceptable, as determined by FDA.

(vi) An appropriate traceability plan to minimize the risk of incorrect results over time, including a description of the molecular size standards and other reagents that may be required for result interpretation, as applicable, that demonstrate the reliable interpretation of the size of the fragments.

(vii) Acceptable, as determined by FDA, device stability protocols and acceptance criteria, that are sufficient to ensure indicated analytical and clinical performance throughout the indicated device stability period. The protocols

and acceptance criteria must be adequate to demonstrate that there is no degradation in signal intensity of full mutations when testing a specimen at the latest indicated time point within the indicated device stability that is comprised of the lowest indicated DNA input that can be used.

Dated: May 22, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–09641 Filed 5–28–25; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2025–N–1160]

Medical Devices; Immunology and Microbiology Devices; Classification of the Zika Virus Serological Reagents

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the Zika virus serological reagents 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 Zika virus serological reagents' 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 29, 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 Zika virus serological reagents 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 (21 U.S.C. 360c(a)(1)). 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 December 26, 2018, FDA received InBios International, Inc.'s request for De Novo classification of the ZIKV Detect 2.0 IgM Capture ELISA. 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