Prevention, by current well-accepted clinical guidelines, or by published peer reviewed research), that the clinical performance is inferior in a specific clinical subpopulation or for a specific claimed specimen type; and

(v) If the device is intended to detect antimicrobial resistance markers, limiting statements, as appropriate, indicating that:

(A) Negative results for claimed resistance markers do not indicate susceptibility of detected microorganisms, as resistance markers not measured by the assay or other potential mechanisms of antibiotic resistance may be present;

(B) Detection of resistance markers cannot be definitively linked to specific microorganisms and the source of a detected resistance marker may be an organism not detected by the assay, including colonizing flora;

(C) Detection of antibiotic resistance markers may not correlate with phenotypic gene expression; and

(D) Therapeutic failure or success cannot be determined based on the assay results, since nucleic acid may persist following appropriate antimicrobial therapy.

(4) Design verification and validation must include:

(i) Detailed device description documentation, including methodology from obtaining sample to result, design of primer/probe sequences, rationale for target sequence 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, Limit of Detection, inclusivity, cross-reactivity, microbial interference, interfering substances, competitive inhibition, carryover/cross contamination, specimen stability, within lab precision, and reproducibility, as appropriate.

(iii) Detailed documentation and performance results from a clinical study that includes prospective (sequential) samples for each claimed specimen type and, when determined to be appropriate by FDA, additional characterized clinical samples. The study must be performed on a study population consistent with the intended use population and compare the device performance to results obtained from FDA accepted comparator methods. Documentation from the clinical studies must include the clinical study protocol (including a predefined statistical analysis plan) study report, testing results, and results of all statistical analyses.

(iv) 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. 2025–08149 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–0725]

Medical Devices; Immunology and Microbiology Devices; Classification of the Cytomegalovirus Nucleic Acid Detection Device for Congenital Cytomegalovirus Infection

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 cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection 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 cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection'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 9, 2025. The classification was applicable on November 30, 2018.

FOR FURTHER INFORMATION CONTACT: Ryan Lubert, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3414, Silver Spring, MD 20993–0002, 240–402–6357, *ryan.lubert@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection 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 July 30, 2018, FDA received Meridian Bioscience, Inc.'s request for De Novo classification of the Alethia CMV Assay Test 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, 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 November 30, 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 866.3181.[1] We have named the generic type of device ''cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection,'' and it is identified as an in vitro diagnostic device intended for the qualitative detection of cytomegalovirus deoxyribonucleic acid (DNA) in clinical samples from newborn babies to aid in the diagnosis of congenital cytomegalovirus infection. Negative results do not preclude infection and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results should be interpreted with consideration of other clinical information and laboratory findings and should not be used as the sole basis for treatment or other patient management decisions.

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—CYTOMEGALOVIRUS NUCLEIC ACID DETECTION DEVICE FOR CONGENITAL CYTOMEGALOVIRUS INFECTION RISKS AND MITIGATION MEASURES

Identified risks to health	Mitigation measures
Risk of false results	General Controls and Special Controls (1) (21 CFR 866.3181(b)(1)) and (2) (21 CFR 866.3181(b)(2)).
Failure to correctly interpret test results.	General Controls and Special Controls (1)(i) (21 CFR 866.3181(b)(1)(i)), (iv) (21 CFR 866.3181(b)(1)(iv)), (v) (21 CFR 866.3181(b)(1)(v)), and (vi) (21 CFR 866.3181(b)(1)(vi)).
Failure to correctly operate the device.	General Controls and Special Controls (1) (21 CFR 866.3181(b)(1)) and (2) (21 CFR 866.3181(b)(2)).

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 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.

[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.

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 § 866.3181 to subpart D to read follows:

§ 866.3181 Cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection.

(a) *Identification.* A cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection is an in vitro diagnostic device intended for the qualitative detection of cytomegalovirus DNA in clinical samples from newborn babies to aid in the diagnosis of congenital cytomegalovirus infection. Negative results do not preclude infection and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results should be interpreted with consideration of other clinical information and laboratory findings and should not be used as the sole basis for treatment or other patient management decisions.

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

(1) 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, the type of results provided to the user, the clinical indications appropriate for test use, and the specific population(s) to be tested.

(ii) A detailed device description, including all device components, instrument requirements, ancillary reagents required but not provided, and an explanation of the methodology, including all pre-analytical methods for specimen processing.

(iii) Performance characteristics from analytical and clinical studies required under paragraphs (b)(2)(ii) and (iii) of this section.

(iv) A detailed explanation of the interpretation of results and criteria for validity of results.

(v) A limiting statement that device results are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions.

(vi) As applicable, a limiting statement and specific sample collection recommendations to indicate that breast milk can result in false positive results for saliva samples if samples are collected less than 1 hour after breastfeeding. Sample collection a minimum of 1 hour from breastfeeding must be recommended.

(vii) Detailed instructions for use that minimize the risk of generating a false result.

(2) Design verification and validation must include:

(i) Detailed device description documentation, including methodology from obtaining sample to result, design of primer/probe sequences, rationale for sequence 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 characterization of the cutoff, analytical sensitivity (limit of detection), inclusivity, reproducibility, interference, cross reactivity, instrument and method carryover/cross contamination, and sample stability and handling.

(iii) Detailed documentation from a clinical study documenting sensitivity and specificity of the device; if the number of positive samples in the clinical study is insufficient to properly estimate device sensitivity, additional pre-selected positive samples must be evaluated to supplement the study. Clinical study subjects must be consistent with the intended use population (*i.e.,* infants younger than 21 days of age), and device results must be compared to FDA-accepted comparator methods. Documentation from the clinical study must include the clinical study protocol, the clinical study report, testing results, and results of all statistical analyses.

(iv) Detailed documentation for device software, including software applications and hardware-based devices that incorporate software.

Dated: May 5, 2025.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–08146 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–0813]

Medical Devices; Immunology and Microbiology Devices; Classification of the Device To Detect and Identify Microbial Nucleic Acids by Fluorescence In Situ Hybridization in Clinical Specimens

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 device to detect and identify microbial nucleic acids by fluorescence in situ hybridization (FISH) in clinical specimens 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 identify microbial nucleic acids by FISH in clinical specimens 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 August 18, 2017.

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 identify microbial nucleic acids by FISH in clinical specimens 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