November 30, 2018

Meridian Bioscience, Inc.
Jack Rogers
Director of Regulatory Affairs and Design Assurance
3471 River Hills Drive
Cincinnati, Ohio 45244

Re: DEN180040
Trade/Device Name: Alethia CMV Assay Test System
Regulation Number: 21 CFR 866.3181
Regulation Name: Cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection
Regulatory Class: Class II
Product Code: QDZ
Dated: July 27, 2018
Received: July 30, 2018

Dear Jack Rogers:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the Alethia CMV Assay Test System, a prescription device with the following indications for use:

> The Alethia CMV Assay Test System includes separately provided test kits for the Alethia CMV DNA Amplification Assay and the Alethia CMV External Control Reagents.
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> The Alethia CMV DNA Amplification Assay, performed on the Alethia instrument, is a qualitative, in vitro diagnostic test system for the direct detection of Cytomegalovirus (CMV) DNA in saliva samples from neonates younger than 21 days of age. The test is used as an aid in the diagnosis of congenital CMV infection. The results of this test should be used in conjunction with the results of other clinical findings.
>
> Flocked swabs should be used to collect saliva from neonates. The swab can be collected dry, without viral transport media (VTM), or placed in no more than 1 mL VTM.
>
> The Alethia CMV External Control Reagents are used as part of a routine quality control program to aid the user in detection of unexpected conditions that may lead to test errors. The external controls are intended for use with the Alethia CMV DNA Amplification Assay; the controls are not intended for use with other assays or systems.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov. FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Alethia CMV Assay Test System and substantially equivalent devices of this generic type, into Class II under the generic name Cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection.

FDA identifies this generic type of device as:

> **Cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection.** 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.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On July 30, 2018, FDA received your De Novo requesting classification of the Alethia CMV Assay Test System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Alethia CMV Assay Test System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the Alethia CMV Assay Test System can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Mitigation Measures
Risk of false results	General controls and Special Controls (1) and (2)
Failure to correctly interpret test results	General Controls and Special Controls 1(i), (iv), (v), (vi)

Identified Risks to Health	Mitigation Measures
Failure to correctly operate the device	General Controls and Special Controls (1) and (2)

In combination with the general controls of the FD&C Act, the cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection is subject to the following special controls:

Special Controls

1. The 21 CFR 809.10 labeling 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 (b)(2)(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 one hour after breastfeeding. Sample collection a minimum of one 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 but not limited to, 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

Special Controls

result).

(ii) Detailed documentation of analytical studies including but not limited to, characterization of the cut-off, analytical sensitivity (limit of detection), inclusivity, reproducibility, interference, cross reactivity, instrument and method carryover/cross contamination, 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, but not limited to, software applications and hardware-based devices that incorporate software.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the cytomegalovirus nucleic acid detection device for congenital cytomegalovirus infection they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Haja Sittana El Mubarak at 301-796-6193.

Sincerely,

Uwe Scherf -S

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health