November 9, 2022

PerkinElmer Inc.
Casey Fox, Ph.D.
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940 Winter Street
Waltham, MA 02451

Re: DEN200044
Trade/Device Name: Eonis™ SCID-SMA Kit
Regulation Number: 21 CFR 866.5980
Regulation Name: Spinal Muscular Atrophy newborn screening test system
Regulatory Class: Class II
Product Code: QUE
Dated: July 7, 2020
Received: July 8, 2020

Dear Dr. Fox:

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 Eonis™ SCID-SMA Kit , a prescription device with the following indications for use:

> The Eonis™ SCID-SMA kit is intended for the qualitative detection of the SMN1 gene exon 7 as an aid in screening newborns for Spinal Muscular Atrophy (SMA). The test is intended for DNA from blood specimens dried on a filter paper and for use on the QuantStudio™ Dx Real-Time PCR instrument.
>
> This test is only intended for use for screening of SMA that bear the homozygous deletion of SMN1 exon 7.
>
> This test is not intended for use as a diagnostic test and a positive screening result should be followed by confirmatory testing.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Eonis™ SCID-SMA Kit, and substantially equivalent devices of this generic type, into Class II under the generic name Spinal Muscular Atrohpy newborn screening test system.

FDA identifies this generic type of device as:

> **Spinal Muscular Atrophy newborn screening test system**. A Spinal Muscular Atrophy (SMA) newborn screening test system is a prescription device intended to detect homozygous deletion of

exon 7 or other similar mutations in the SMN1 (Survival Motor Neuron 1) gene of DNA obtained from dried blood spot specimens on filter paper using a polymerase chain reaction-based test as an aid in screening newborns for SMA. Presumptive positive results are intended to be followed up by diagnostic confirmatory testing.

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 8, 2020, FDA received your De Novo requesting classification of the Eonis™ SCID-SMA Kit. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Eonis™ SCID-SMA Kit 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 Eonis™ SCID-SMA Kit 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:

Table 1 – Identified Risks to Health and Identified Mitigations

Identified Risks to Health	Mitigation Measures
Risk of false negative results	Certain design verification and validation identified in special control (1), including certain device description information and documentation of certain analytical studies and clinical studies Certain labeling information identified in special control (2), including limitations, device descriptions, explanation of procedures, and performance information
Risk of false positive results	Certain design verification and validation identified in special control (1), including certain device description information and

	documentation of certain analytical studies and clinical studies Certain labeling information identified in special control (2), including limitations, device descriptions, explanation of procedures, and performance information

In combination with the general controls of the FD&C Act, the Spinal Muscular Atrophy newborn screening test system is subject to the following special controls:

1) Design verification and validation must include the following:

(i) A detailed device description, including all device parts (e.g., instruments and associated user manuals, device software, reagents, calibrators, controls, and consumables) and their use within the testing procedure.

(ii) A detailed explanation of the technology, method(s) of data processing from signal acquisition to result assignment, and pre-specified cut-offs used to interpret the data and generate results and sample reports.

(iii) A description of appropriate internal and external controls that are recommended or provided. The description must identify those control elements that are incorporated into the testing procedure.

(iv) Detailed specifications for the filter paper to be used as part of the device, which must be appropriately labeled for in vitro diagnostic use. Specifications must include punch size and address any properties of the filter paper that may interfere with obtaining test results.

(v) Detailed documentation of the following analytical and clinical studies, including the study protocols containing descriptions of the test methods, prescribed methods of data analysis and acceptance criteria, final study reports, and data line listings:

(A) A study demonstrating the clinical performance of the device using well characterized prospectively or retrospectively obtained clinical specimens from the intended use population and include homozygous and heterozygous specimens of sufficient number to be determined to be acceptable to FDA. Confirmed positive specimens must have a diagnosis based on confirmatory diagnostic methods. The confirmed positives must include samples from SMA types 1-4. Additionally, samples with SMN2 copy number ranging to 4 must be evaluated to determine the risk of false negative (unaffected) results due to assay cross reactivity with the SMN2 gene. A description of the sample collection strategy and accountability must be

included. Specimens used in the study must be from patients other than those used to design the test, and validation testing must be based on a pre-specified clinical decision point (i.e., cutoff to distinguish positive and negative results). Results must be summarized in a tabular format comparing interpretation of results to the reference method. Point estimates together with two-sided 95 percent confidence intervals must be provided for the positive percent agreement (sensitivity) and negative percent agreement (specificity). Data must include the retest rate, false positive rate before retest, final false positive rate, and false negative rate. Positive predictive value (PPV) and negative predictive value (NPV) must be provided based on published reference to prevalence in the target population.

(B) A study demonstrating device accuracy in comparison to the results obtained by a reference or comparator method determined to be acceptable by FDA.

(C) A study demonstrating device reproducibility generated using a minimum of three sites, of which at least two must be external sites, with at least two operators at each site using the specified extraction method(s) and protocol. The evaluation must include multiple runs, days, different instruments, and different reagent lots. The study must include heterozygous deleted, homozygous deleted, and unaffected specimens. Identical specimens from the same sample panel must be tested at each site. Results must be summarized in a tabular format and reported as standard deviation and 95 percent confidence intervals for the quantitative result and agreement for qualitative results for between-site, between-operator, between-day/run, and within-run (repeatability) for each specimen.

(D) A lot-to-lot reproducibility study of each filter paper intended to be used with the test. The lot-to-lot study must include a minimum of three lots of each blood spot card that will be validated with the test and be conducted over five nonconsecutive days. The sample panel must consist of at least one positive and one negative specimen. Multiple punches must be obtained from each card for demonstration of homogeneity of the analyte across the dried blood spot. Comparability of the test performance for each filter paper must be demonstrated. Stability and storage of SMN1 DNA on each blood spot card must be demonstrated. Results of the lot-to-lot study must be summarized by providing the agreement within replicates on the assay final result for positive and negative specimens with pre-specified acceptance criteria and 95 percent confidence intervals for all data. Data must be calculated for within-lot and between-lot reproducibility. Data demonstrating the concordance between results across different filter papers must be provided. Study acceptance criteria must be provided and followed.

(E) A study demonstrating device specificity, including interference, carryover/cross-contamination, and analysis of potential off-target genomic sequences, including evaluation of SMN2 amplification, to evaluate the risk of clinically false negative or false positive results.

(F) Studies performed to support the stability of samples using the indicated specimen collection method(s) under various storage times, temperatures, and freeze-thaw conditions, as applicable.

(G) Studies performed to demonstrate on-board and in-use reagent stability, including the test method(s), data analysis plans, acceptance criteria, final study reports, and data line listings. Such documentation should include studies to demonstrate reagent shelf-life for the assay kit, including study protocols containing descriptions of the test method(s), data analysis plans, and acceptance criteria.

(H) Studies performed to evaluate the risk of false positive and false negative results (e.g., validation of the cycle thresholds or other metric, as applicable, used to define the assay reportable range when assessing a range of DNA input, equivalency of different filter paper, and the limit of blank, when determined appropriate by FDA).

(I) A shipping stability study, separate from the study described in paragraph (1)(vi)(G), must be performed that demonstrates acceptable stability of the parts that comprise the kit.

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

(vii) Identification of all 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 using the device.

2) The labeling required under 21 CFR 809.10(b) must include:

(i) An intended use statement that includes:

(A) A detailed description of the target(s) the device detects; and

(B) The clinical indications appropriate for test use.

(ii) Prominent and conspicuous limiting statements clearly explaining:

(A) This test is not intended to screen for SMA subtypes other than those specifically stated in the intended use, nor is it intended for carrier screening, as a stand-alone diagnostic test, or for determining eligibility for therapeutic products.

(B) Test results are intended to be used in conjunction with other clinical and diagnostic findings, consistent with professional standards of practice, including confirmation of presumptive positive results by diagnostic confirmatory testing and clinical evaluation, as appropriate.

(iii) Description of the device information required under paragraphs (1)(i-iv).

(iv) A summary of the results of the studies required under paragraphs 1(v)(A-G).

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.

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 Spinal Muscular Atrohpy newborn screening test system 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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-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 Allen Williams at 301-796-4806.

Sincerely,

Donna M. Roscoe -S

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Acting Director, Division of Molecular Genetics and Pathology
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