May 18, 2023

BRAHMS GmbH, Part of Thermo Fisher Scientific
Anja Jagalla
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Germany

Re: DEN220027
Trade/Device Name: B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR Test System
Regulation Number: 21 CFR 862.1602
Regulation Name: Prognostic test for development or progression of preeclampsia
Regulatory Class: Class II
Product Code: QWH
Dated: April 29, 2022
Received: May 2, 2022

Dear Anja Jagalla:

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 B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR Test System:

The B·R·A·H·M·S™ sFlt-1/ PlGF KRYPTOR™ Test System is comprised of the B·R·A·H·M·S PlGF plus KRYPTOR assay and the B·R·A·H·M·S sFlt-1 KRYPTOR assay.

The B·R·A·H·M·S PlGF plus KRYPTOR is an automated immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE™) technology for the quantitative determination of the concentration of Placental Growth Factor (PlGF) in human serum and plasma (K2 EDTA) on the B·R·A·H·M·S KRYPTOR analyzer.

The B·R·A·H·M·S sFlt-1 KRYPTOR is an automated immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE) technology for the quantitative determination of the concentration of soluble fms-like tyrosine kinase-1 (sFlt-1), also known as VEGF receptor-1, in human serum and plasma (K2 EDTA) on the B·R·A·H·M·S KRYPTOR analyzer.

The B·R·A·H·M·S PlGF plus KRYPTOR is to be used in conjunction with the B·R·A·H·M·S sFlt-1 KRYPTOR along with other laboratory tests and clinical assessments to aid in the risk assessment of pregnant women (singleton pregnancies between gestational age 23+0 to 34+6/7 weeks) hospitalized for hypertensive disorders of pregnancy

(preeclampsia, chronic hypertension with or without superimposed preeclampsia, or gestational hypertension) for progression to preeclampsia with severe features (as defined by the American College of Obstetricians and Gynecologists (ACOG) guidelines) within 2 weeks of presentation.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR Test System, and substantially equivalent devices of this generic type, into Class II under the generic name prognostic test for development or progression of preeclampsia.

FDA identifies this generic type of device as:

Prognostic test for development or progression of preeclampsia. A prognostic test for development or progression of preeclampsia is an in vitro diagnostic device intended to measure one or more analytes obtained from human samples. A prognostic test for development or progression of preeclampsia is indicated as an aid in the risk assessment for the development or progression of preeclampsia. This device is not intended for diagnosis of any disease.

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 May 2, 2022, FDA received your De Novo requesting classification of the B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR Test System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR 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 B·R·A·H·M·S sFlt-1/ PlGF KRYPTOR 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:

Risks to Health	Mitigation Measures
Incorrect performance of the test leading to false positive results	Certain design verification and validation activities and documentation. Certain labeling information, including certain limiting statements and performance characteristics.
Incorrect interpretation of test results	Certain design verification and validation activities, including certain licensed practitioner training as part of risk management activities. Certain labeling information, including certain limiting statements.

In combination with the general controls of the FD&C Act, the prognostic test for development or progression of preeclampsia is subject to the following special controls:

(1) Design verification and validation must include:

i. Detailed documentation of a study that demonstrates the clinical performance of the device for its intended use, evaluated across multiple intended use sites and broad demographics representative of intended use patients in the United States; or through an alternative approach determined to be appropriate by FDA;

ii. Detailed documentation of studies that demonstrate the analytical performance of the device for its intended use, including for each analyte and device output. These studies must include precision, reproducibility, metrological accuracy, and analytical specificity studies, or alternative approaches determined to be appropriate by FDA; and

iii. As part of the risk management activities, documentation of an appropriate licensed practitioner training program on the proper use of the device and proper interpretation of results that must be offered to licensed practitioners, or an alternative approach determined to be appropriate by FDA.

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

i. Detailed descriptions of the device studies demonstrating the performance of the device, including results; and

ii. Limiting statements including the following:

A. The test result is intended as an aid in the management of the patient, and not to be used to replace clinical judgement.

B. The test result is not to be used to aid in the diagnosis of preeclampsia or conditions resulting from progression of preeclampsia.

C. The test result is not to be used to aid in decisions of hospital discharge.

D. The test result is not to be used to aid in decisions of pregnancy delivery.

E. The test is not intended to inform the healthcare provider about whether or not changes in immediate treatment, including medication or hospitalization, are needed.

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 prognostic test for development or progression of preeclampsia 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 Part 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 Jonathan Leland at 240-402-1847.

Sincerely,

Marianela Perez-torres -S

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