



Food and Drug Administration  
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July 22, 2016

Asuragen, Inc.  
Fayyaz Memon  
Vice President, Regulatory and Clinical Affairs, Quality Assurance  
2170 Woodward St.  
Austin, TX 78744-1840

Re: DEN160003  
QuantideX qPCR BCR-ABL IS Kit  
Evaluation of Automatic Class III Designation – *De Novo* Request  
Regulation Number: 21 CFR 866.6060  
Regulation Name: BCR-ABL Quantitation Test  
Regulatory Classification: Class II  
Product Code: OYX  
Dated: January 19, 2016  
Received: January 19, 2016

Dear Mr. Memon:

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 QuantideX qPCR BCR-ABL IS Kit, a prescription device. The indications for use of the QuantideX qPCR BCR-ABL IS Kit is:

The QuantideX qPCR BCR-ABL IS Kit is an in vitro nucleic acid amplification test for the quantitation of BCR-ABL1 and ABL1 transcripts in total RNA from whole blood of diagnosed t(9;22) positive Chronic Myeloid Leukemia (CML) patients expressing BCR-ABL1 fusion transcripts type e13a2 and/or e14a2. The QuantideX qPCR BCR-ABL IS Kit is a reverse transcription-quantitative PCR performed on the Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument and is intended to measure BCR-ABL1 to ABL1, expressed as a log molecular reduction (MR value) from a baseline of 100% on the International Scale, in t(9;22) positive CML patients during monitoring of treatment with Tyrosine Kinase Inhibitors (TKIs).

The test does not differentiate between e13a2 or e14a2 fusion transcripts and does not monitor other rare fusion transcripts resulting from t(9;22). This test is not intended for the diagnosis of CML.

FDA concludes that this device, and substantially equivalent device of this generic type, should be classified into class II. This order, therefore, classifies the QuantideX qPCR BCR-ABL IS Kit and substantially equivalent devices of this generic type, into class II under the generic name, “BCR-ABL Quantitation Test.”

FDA identifies this generic type of device as: **BCR-ABL Quantitation Test.**

A BCR-ABL Quantitation Test is a reverse transcription-quantitative polymerase chain reaction (RT-qPCR) test for the quantitation of BCR-ABL1 expressed on the International Scale and control transcripts in total RNA from whole blood of diagnosed t(9;22) positive Chronic Myeloid Leukemia (CML) patients during monitoring of treatment with Tyrosine Kinase Inhibitors (TKIs). This test is not intended for the diagnosis of CML.

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 new 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, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. 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** classifying the device type.

On January 19, 2016, FDA received your *de novo* requesting classification of the QuantideX qPCR BCR-ABL IS Kit into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the QuantideX qPCR BCR-ABL IS 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 the QuantideX qPCR BCR-ABL IS Kit indicated for use as follows:

The QuantideX qPCR BCR-ABL IS Kit is an in vitro nucleic acid amplification test for the quantitation of BCR-ABL1 and ABL1 transcripts in total RNA from whole blood of diagnosed t(9;22) positive Chronic Myeloid Leukemia (CML) patients expressing BCR-ABL1 fusion transcripts type e13a2 and/or e14a2. The QuantideX qPCR BCR-ABL IS Kit is a reverse transcription-quantitative PCR performed on the Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument and is intended to measure BCR-ABL1 to ABL1, expressed as a log molecular reduction (MR value) from a baseline of 100% on the International Scale, in t(9;22) positive CML patients during monitoring of treatment with Tyrosine Kinase Inhibitors (TKIs).

The test does not differentiate between e13a2 or e14a2 fusion transcripts and does not monitor other rare fusion transcripts resulting from t(9;22). This test is not intended for the diagnosis of CML.

can be classified in class II with the establishment of special controls for this type of device.

FDA believes that the class II special controls identified later in this order, along with applicable general controls, including the design controls under 21 CFR part 820, provide reasonable assurance of the safety and effectiveness of the device type.

**Table 1– Identified Risks and Required Mitigations**

<b>Identified Risks to Health</b>	<b>Required Mitigations</b>
False negative results	Special Controls (1) and (2)
False positive results	Special Controls (1) and (2)
Lack of traceability of results	Special Control (3)

In combination with the general controls of the FD&C Act, a BCR-ABL Quantitation Test is subject to the following special controls:

- (1) Premarket notification submissions must include the following information:
  - (i) The indication for use must indicate the variant(s) for which the assay was designed and validated, for example BCR-ABL e13a2 and/or e14a2.
  - (ii) A detailed description of all components in the test, including the following:
    - (A) A detailed description of the test components, all required reagents, instrumentation and equipment, including illustrations or photographs of non-standard equipment or methods.
    - (B) Detailed documentation of the device software including, but not limited to, standalone software applications and hardware-based devices that incorporate software.
    - (C) Methodology and protocols for control procedures for the assay to allow reporting on the International Scale.
    - (D) A description of the result outputs, analytical sensitivity of the assay, and the range of values that will be reported.
    - (E) 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.
  - (iii) Information that demonstrates the performance characteristics of the test, including:
    - (A) For indications for use based on a threshold established in a predicate device of this generic type, device performance data from either a method comparison study to the predicate device or through a clinical study demonstrating clinical validity using well-characterized prospectively or retrospectively obtained clinical specimens, as appropriate, representative of the intended use population.
    - (B) For indications for use based on a threshold not established in a predicate device of this generic type, device performance data from a clinical study demonstrating clinical validity using well characterized prospectively or retrospectively obtained clinical specimens, as appropriate, representative of the intended use population.
    - (C) Device reproducibility data generated, using a minimum of three sites,

of which at least two sites must be external sites, with two operators at each site. Each site must conduct a minimum of 3 runs per operator over non-consecutive days evaluating a minimum of 5 different BCR-ABL concentrations that span and are well distributed over the measuring range and include MR3 (0.1% IS). Results shall be reported as the standard deviation and percentage coefficient of variation for each level tested. Pre-specified acceptance criteria must be provided and followed.

- (D) Device precision data using clinical samples to evaluate the within-lot, between-lot, within-run, between run, and total variation.
  - (E) Device linearity data using a dilution panel created from clinical samples.
  - (F) Device analytic sensitivity data, including limit of blank, limit of detection, and limit of quantification.
  - (G) Device specificity data, including interference and cross-contamination.
  - (H) Device stability data, including real-time stability of samples under various storage times, temperatures, and freeze-thaw conditions
- (iv) Identification of risk mitigation elements used by your device, including a detailed description of all additional procedures, methods, and practices incorporated into the instructions for use that mitigate risks associated with testing using your device.
- (2) Your 21 CFR 809.10 compliant labeling must include the following:
    - (i) The intended use in your 21 CFR 809.10(a)(2) and 21 CFR 809.10(b)(2) complaint labeling must include an indication for use statement that reads “This test is not intended for the diagnosis of CML.”
    - (ii) A detailed description of the performance studies conducted to comply with section (1)(iii) and a summary of the results.
  - (3) Your device output must include results on the International Scale (%IS) and your assay must include multi-point calibration controls traceable to a relevant international reference panel (e.g., the World Health Organization (WHO) International Genetic Reference Panel for quantitation of BCR-ABL mRNA).

In addition, this is a prescription device. 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 BCR-ABL Quantitation Test they intend to market prior to marketing the device and receive clearance to market from FDA.

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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); 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.

If you have any questions concerning this classification order, please contact Jennifer Dickey at 301-796-5028.

Sincerely yours,

Reena Philip, Ph.D.  
Director  
Division of Molecular Genetics and Pathology  
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