



Food and Drug Administration
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March 28, 2017

QIAGEN Manchester Ltd.
Claire Ryan
Senior Manager, Regulatory Affairs
Skelton House
Lloyd Street North
Manchester, M15 6SH, UK

Re: DEN160028
ipsogen[®] JAK2 RGQ PCR Kit
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 866.6070
Regulation Name: Mutation detection test for myeloproliferative neoplasms
Regulatory Classification: Class II
Product Code: PSU
Dated: June 30, 2016
Received: July 1, 2016

Dear Ms. Ryan:

This letter corrects our letter sent March 27, 2017 and dated March 27, 2017.

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 *ipsogen* JAK2 RGQ PCR Kit, a prescription device. The *ipsogen* JAK2 RGQ PCR Kit is indicated for use as follows:

The *ipsogen* JAK2 RGQ PCR Kit is a qualitative in vitro diagnostic test for the detection of the JAK2 V617F/G1849T allele in genomic DNA extracted from EDTA whole blood. The *ipsogen* JAK2 RGQ PCR Kit is a real time PCR test performed on the QIAGEN Rotor-Gene Q MDx instrument. The test is intended for use as an adjunct to evaluation of suspected Polycythemia Vera, in conjunction with other clinicopathological factors.

This test does not detect less common mutations associated with Polycythemia Vera including mutations in exon 12 and is not intended for stand-alone diagnosis of Polycythemia Vera.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the *ipsogen* JAK2 RGQ PCR Kit, and substantially equivalent devices of this generic type, into class II under the generic name, “Mutation detection test for myeloproliferative neoplasms.”

FDA identifies this generic type of device as: **Mutation detection test for myeloproliferative neoplasms.**

A mutation detection test for myeloproliferative neoplasms is an in vitro diagnostic device intended for the detection of the JAK2 V617F/G1849T allele in genomic DNA extracted from whole blood. The test is intended for use as an adjunct to evaluation of suspected Polycythemia Vera, in conjunction with other clinicopathological factors.

Section 513(f)(2) of the Food, Drug & Cosmetic Act (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 FD&C 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 FD&C 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 FD&C 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 July 1, 2016, FDA received your *de novo* requesting classification of the *ipsogen* JAK2 RGQ PCR Kit into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the *ipsogen* JAK2 RGQ PCR 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 *ipsogen* JAK2 RGQ PCR Kit indicated for use as follows:

The *ipsogen* JAK2 RGQ PCR Kit is a qualitative in vitro diagnostic test for the detection of the JAK2 V617F/G1849T allele in genomic DNA extracted from EDTA whole blood. The *ipsogen* JAK2 RGQ PCR Kit is a real time PCR test performed on the QIAGEN Rotor-Gene Q MDx instrument. The test is intended for use as an adjunct to evaluation of suspected Polycythemia Vera, in conjunction with other clinicopathological factors.

This test does not detect less common mutations associated with Polycythemia Vera including mutations in exon 12 and is not intended for stand-alone diagnosis of Polycythemia Vera.

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. The identified risks to health and identified mitigations associated with the device type are summarized in Table 1.

Table 1 – Identified Risks to Health and Required Mitigations

Identified Risks to Health	Required Mitigations
False negative results	Special Controls (1) and (2)
False positive results	Special Controls (1) and (2)

In combination with the general controls of the FD&C Act, a mutation detection test for myeloproliferative neoplasms is subject to the following special controls:

(a) *Identification.* A mutation detection test for myeloproliferative neoplasms is an in vitro diagnostic device intended for the detection of the JAK2 V617F/G1849T allele in genomic DNA extracted from whole blood. The test is intended for use as an adjunct to evaluation of suspected Polycythemia Vera, in conjunction with other clinicopathological factors.

(b) *Classification.* Class II (special controls). A mutation detection test for myeloproliferative neoplasms must comply with the following special controls:

1) Premarket notification submissions must include the following:

- i. The indication for use must indicate the variant(s) for which the assay was designed and validated, for example JAK2 G1849T.
- 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) A detailed description of methodology and assay procedures including appropriate internal and external quality controls that are recommended or provided. The description must identify those control elements that are incorporated into the testing procedure.
 - (D) A detailed specification for sample collection, processing, and storage.
 - (E) A description of the criteria for test result interpretation and reporting including result outputs, analytical sensitivity of the assay, and the values that will be reported.

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 study that includes at least 2 operators per site, 2 runs per operator per day over a minimum of 3 non-consecutive days evaluating a sample panel that contains allelic frequencies that span the claimed measuring range, and include the clinical threshold allelic frequency. Pre-specified acceptance criteria must be provided and followed.
 - (D) Information on device traceability and a description of the value assignment process for calibrators and controls.
 - (E) Device precision data using clinical samples and controls to evaluate the within-lot, between-lot, within-run, between run, and total variation.
 - (F) Device linearity data generated from samples covering the device measuring range and for any standards used in the quantitation of allelic frequencies.
 - (G) Device analytic sensitivity data including limit of blank and limit of detection.
 - (H) Device specificity data, including interference and cross-contamination.
 - (I) Device and clinical specimen stability data, including real-time stability (long term storage and in-use stability) and stability evaluating various storage times, temperatures, and freeze-thaw conditions, as appropriate.
- iv. Identification of 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 testing using the device.
- 2) The 21 CFR 809.10(b) compliant labeling must include a detailed description of the performance studies conducted to comply with section b.1.iii and a summary of the results.

This device is subject to the premarket notification requirements under section 510(k) of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the cellular analysis system for multiplexed antimicrobial susceptibility testing they intend to market and receive clearance to market from FDA 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); 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 Janaki Veeraraghavan at 240-402-6634.

Sincerely,

For Reena Philip, Ph.D.
Director
Division of Molecular Genetics and Pathology
Office of *In Vitro* Diagnostics and Radiological
Health
Center for Devices and Radiological Health