January 12, 2018

QIAGEN, GmbH
c/o Claire Ryan
Senior Manager, Regulatory Affairs
QIAGEN Manchester, LTD
Skelton House, Lloyd Street North
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Re: K172287
Trade/Device Name: *ipsogen*® JAK2 RGQ PCR Kit
Regulation Number: 21 CFR 866.6070
Regulation Name: Mutation detection test for myeloproliferative neoplasms
Regulatory Class: Class II
Product Code: PSU
Dated: December 14, 2017
Received: December 14, 2017

Dear Claire Ryan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 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 Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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).

Sincerely,

Yun-fu Hu -S

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K172287

Device Name
ipsogen JAK2 RGQ PCR Kit

Indications for Use *(Describe)*

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 Myeloproliferative Neoplasm in conjunction with other clinicopathological factors.

This test does not detect less common JAK2 mutations associated with Myeloproliferative Neoplasm including mutations in exon 12 and is not intended for stand-alone diagnosis of Myeloproliferative Neoplasm.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

General Information

Submitted by: QIAGEN GmbH
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Date Prepared: July 28, 2017

Device Name: *ipsogen*® JAK2 RGQ PCR Kit

Trade Name: *ipsogen*® JAK2 RGQ PCR Kit

Common Name: Mutation detection test for myeloproliferative neoplasms

Classification: Class II

Product Code: PSU

Predicate Device

Manufacturer	**Product Name**	**510(k) No.**
QIAGEN GmbH	*ipsogen*® JAK2 RGQ PCR Kit	DEN160028

Device Description

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 whole blood. The *ipsogen* JAK2 RGQ PCR Kit uses polymerase chain reaction (PCR), and ARMS (amplification refractory mutation system) technology on the Rotor-Gene Q MDx instrument.

Samples are extracted and prepared using the QIAsymphony SP instrument (QSSP) with the QIAsymphony® DSP DNA Mini Kit, followed by assay setup amplification and detection are carried out using the *ipsogen J*AK2 RGQ PCR Kit with the Rotor-Gene Q MDx and Rotor-Gene AssayManager software version 2.1.x**, Rotor-Gene AssayManager Gamma MDx plug-in installed, version 1.0.x** and an associated JAK2 Assay profile (from file AP_ipsogen_JAK2_blood_US_ Vx_x_x**.iap).

The extraction step on the QIAsymphony instrument (QSSP) ensures that enough gDNA (of adequate quality) is purified during each run (no repeated extraction for the same sample is expected unless the instrument states that the step failed).

The *ipsogen* JAK2 RGQ PCR Kit is designed to be used with the Rotor-Gene Q MDx (RGQ) instrument which is a real-time PCR analyzer designed for rapid thermal cycling and real-time detection of PCR assays. The Rotor-Gene AssayManager (RGAM) controls and monitors PCR reactions and allows the determination of the mutation status based upon PCR results.

The presence of the JAK2 mutation is indicated by the fluorescent signal generated through the use of fluorescently labeled oligonucleotide probes. The probes do not generate a signal unless they are specifically bound to the amplified product. The amplification cycle at which fluorescent signal is detected by the RGQ MDx is inversely proportional to the DNA target concentration present in the original specimen.

The *ipsogen* JAK2 RGQ PCR Kit contains reagents for two separate PCR reactions: one mutation-specific reaction and one wild-type specific reaction. The reaction mix uses a mutant-specific or wild-type specific primer (Reverse primer), together with a common Forward primer and a labeled probe, to amplify and detect the G1849T mutation or the wild-type sequence in the JAK2 gene.

In addition, each Reaction Mix contains reagents (unlabeled primers, probe and oligonucleotide template) for an internal control reaction. The internal control is designed to be a reaction that does not compete significantly with the mutation-specific or wild-type specific, reaction mixes. and serve to demonstrate that the entire assay process has proceeded correctly for each specimen.

*Note: ** x≥ 0, x corresponds to the latest version available on QIAGEN Website*

Intended Use

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 Myeloproliferative Neoplasms, in conjunction with other clinicopathological factors.

This test does not detect less common JAK2 mutations associated with Myeloproliferative Neoplasms including mutations in exon 12 and is not intended for stand-alone diagnosis of Myeloproliferative Neoplasm.

Comparison of the *ipsogen* JAK2 RGQ PCR Kit and the Predicate Device

The *ipsogen* JAK2 RGQ PCR Kit is substantially equivalent to the predicate device

- DEN160028: *ipsogen* JAK2 RGQ PCR Kit

Similarities and differences between the *ipsogen* JAK2 RGQ PCR Kit and the predicate device are shown in Table 1.

Table 1: Comparison of the *ipsogen* JAK2 RGQ PCR Kit with the Predicate Device

Characteristic	Device	Predicate
Similarities		
Specimen Type	genomic DNA extracted from EDTA whole blood	genomic DNA extracted from EDTA whole blood
Assay Targets	JAK2 V617F/G1849T allele	JAK2 V617F/G1849T allele
Genomic DNA Extraction	DNA should be extracted using the QIAsymphony SP instrument in combination with the QIAsymphony DSP DNA Mini Kit	DNA should be extracted using the QIAsymphony SP instrument in combination with the QIAsymphony DSP DNA Mini Kit
Amplification and Detection Technology	Real-time PCR DNA amplification	Real-time PCR DNA amplification

Characteristic	Device	Predicate
Amplification and Detection Instrument System	Assay uses the Rotor-Gene Q MDx	Assay uses the Rotor-Gene Q MDx
Assay Controls	Positive Control, Negative Control and Internal Control included in the kit.	Positive Control, Negative Control and Internal Control included in the kit.
Differences		
Intended Use	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 Myeloproliferative Neoplasms, in conjunction with other clinicopathological factors. This test does not detect less common JAK2 mutations associated with Myeloproliferative Neoplasms including mutations in exon 12 and is not intended for stand-alone diagnosis of Myeloproliferative Neoplasms.	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.
Amplification and Detection Instrument System Software	• Rotor-Gene AssayManager® software version 2.1.x** • Rotor-Gene AssayManager Gamma MDx plug-in installed, version 1.0.x** • JAK2 Assay Profile (from file AP_ipsogen_JAK2_blood_US_ Vx_x_x**iap) *(** x≥ 0, x corresponds to the latest version available on QIAGEN Website)*	• Rotor-Gene AssayManager® software version 1.0.x (where x is greater than or equal to 4) • Rotor-Gene AssayManager JAK2 plug-in installed, version 1.0.x (where x is greater than or equal to 2) • JAK2 Assay Profile (from file AP_ipsogen_JAK2_blood_US_V1.0.0.iap)

The differences between the *ipsogen* JAK2 RGQ PCR Kit and the predicate device are the broader intended use statement which has been extended to include the evaluation of patients with suspected Myeloproliferative Neoplasms in addition to Polycythemia Vera and the software following the release of the updated Rotor Gene Assay Manager (RGAM) software. This includes the update to the Rotor-Gene AssayManager software, the Rotor-Gene AssayManager Gamma MDx plug-in and the JAK2 Assay Profile. The updated software includes updates to invalidating sample flags, however there is no change to the automated data analysis and interpretation of the results for the *ipsogen* JAK2 RGQ PCR Kit.

These differences do not affect substantial equivalency of the *ipsogen* JAK2 RGQ PCR Kit and the predicate device. Both assays detect the JAK2 V617F/G1849T allele in genomic DNA extracted from EDTA whole blood using the QIAGEN Rotor-Gene Q MDx instrument. The differences noted above do not raise questions of safety and effectiveness because both assays use the same controls, follow the same workflow for the same purpose of DNA extraction, assay setup, and Real-time PCR DNA amplification.

Therefore, the *ipsogen* JAK2 RGQ PCR Kit is substantially equivalent to the legally marked predicate device listed.

Performance Characteristics - Non-Clinical Studies in this 510(k)

Analytical Accuracy

The purpose of this study was to validate the analytical accuracy of the *ipsogen* JAK2 RGQ PCR Kit under condition of normal use on clinical samples from subjects suspected of having myeloproliferative neoplasms. This study was performed on gDNA samples extracted from a total of 473 specimens: 276 with suspected PV, 98 with ET and 99 with PMF. The JAK2 V617F status of the patient samples obtained with the ipsogen JAK2 RGQ PCR kit were compared with the JAK2 V617F status obtained with the reference method for JAK2 status determination, i.e. an independently validated bi-directional sequencing (BDS). Of the 473 specimens 15 specimens were JAK2 positive by the *ipsogen* JAK2 RGQ PCR kit while negative by BDS.

The overall agreement is 96.8% (458/473 subjects; 95% CI: [94.8%; 98.2%]). The positive agreement was 100% (165/165 subjects; 95%CI: [97.8%; 100%] and the negative agreement was 95.1 % (293/308 subjects; 95% CI: [92.1%; 97.2 %]). The results are shown in Table 2.

Table 2: Concordance table between *ipsogen* JAK2 RGQ PCR Kit and Sanger Bidirectional Sequencing in MPN population (combined ET, PMF and PV populations)

		Sanger bi-directional sequencing		Total
		JAK2 V617F positive	JAK2 V617F negative	
ipsogen JAK2 RGQ PCR Kit	JAK2 V617F positive	165	15	180
	JAK2 V617F negative	0	293	293
	Total	165	308	473

Assessment of analytical accuracy study results in MPN cohorts

The overall concordance between results obtained for the JAK2 V617F mutation with the *ipsogen* JAK2 RGQ PCR Kit and with Sanger sequencing (BDS) in subjects with ET, PMF and PV are provided separately:

For ET, the overall agreement is 90.8% (89/98 subjects; 95% CI: [83.3% – 95.7%]), the positive agreement is 100% (43/43 subjects; 95% CI: [91.8% – 100%]), and the negative agreement is 83.6% (46/55 subjects; 95% CI: [71.2% – 92.2%]).

For PMF, the overall agreement is 94.9% (94/99 subjects; 95% CI: [88.6% – 98.3%]), the positive agreement is 100% (51/51 subjects; 95% CI: [93.0% – 100%]), and the negative agreement is 89.6% (43/48 subjects; 95% CI: [77.3% – 96.5%]).

For PV, the overall agreement is 99.6% (275/276 subjects; 95% CI: [98.0% – 100%]), the positive agreement is 100% (71/71 subjects; 95% CI: [94.9% – 100%]), and the negative agreement is 99.5% (204/205 subjects; 95% CI: [97.3% – 100%]).

The specimens yielding discordant results appeared to have mutation levels below the BDS detection capability (around 10%). Because Sanger sequencing is not as sensitive as the JAK2 assay, and the JAK2 assay reporting ≥ 1%, a separate study was conducted using a validated next generation sequencing (NGS) method to detect JAK2 V617F allele in the 15 discordant samples (9 ET, 5 PMF, and 1 PV), as well as a randomly selected set of 22 JAK2 V617F positive and negative concordant specimens. All 15 discordants tested positive by NGS, agreeing with the *ipsogen* JAK2 RGQ PCR Kit. All concordant samples tested the same with NGS and in agreement with the *ipsogen* JAK2 RGQ PCR Kit and BDS .

Conclusion of the analytical accuracy study

The *ipsogen* JAK2 RGQ PCR Kit was 100% accurate for the detection of JAK2 V617F allele in specimens from subjects with JAK2 V617F levels ≥1%.

Conclusions

The *ipsogen* JAK2 RGQ PCR Kit is substantially equivalent to the legally marketed QIAGEN *ipsogen* JAK2 RGQ PCR Kit.