effect on the performance of this test has not been studied.''

(D) Analytical sensitivity data: data must be provided demonstrating the minimum amount of DNA that will enable the test to perform correctly in 95 percent of runs.

(E) Device stability data: the manufacturer must establish upper and lower limits of input nucleic acid, sample, and reagent stability that will achieve the test's claimed accuracy and reproducibility. The manufacturer must evaluate stability using wild-type, heterozygous, and homozygous samples. Data supporting such claims must be provided.

(F) Specimen type and matrix comparison data: specimen type and matrix comparison data must be generated if more than one specimen type can be tested with this device, including failure rates for the different specimens.

(xiii) Clinical Performance Summary.

(A) Information to support the clinical performance of each variant in the specific condition which is labeled as ''are associated with increased risk'' and reported by the test must be provided, as identified in paragraph (b)(4)(iii)(C) of this section.

(B) Manufacturers must organize information by the specific variant combination as appropriate (*e.g.,* wild type, heterozygous, homozygous, compound heterozygous, hemizygous genotypes). For each variant combination, information must be provided in the clinical performance section to support clinical performance for the risk category (*e.g.,* not at risk, increased risk). For each variant combination, a summary of key results must be provided in tabular format or using another method identified as appropriate by FDA to include the appropriate information regarding variant type, data source, definition of the target condition (*e.g.,* disease), clinical criteria for determining whether the target disease is present or absent, description of subjects with the target disease present and target disease absent (exclusion or inclusion criteria), and technical method for genotyping. When available, information on the effect of the variant on risk must be provided as the risk of a disease (lifetime risk or lifetime incidences) for an individual compared with the general population risk.

(xiv) User comprehension study: information on a study that assesses comprehension of the test process and results by potential users of the test must be provided, including the following, as appropriate:

(A) The test manufacturer must provide a genetic health risk education module to naïve user comprehension study participants prior to their participation in the user comprehension study. The module must define terms that are used in the test reports and explain the significance of genetic risk reports.

(B) The test manufacturer must perform pre- and post-test user comprehension studies. The comprehension test questions must directly evaluate the material being presented to the user as described in paragraph (b)(3)(ii) of this section.

(C) The manufacturer must provide a justification from a physician and/or genetic counselor that identifies the appropriate general and variant-specific concepts contained within the material being tested in the user comprehension study to ensure that all relevant concepts are incorporated in the study.

(D) The user comprehension study must meet the following criteria:

(1) The study participants must comprise a statistically sufficient sample size and demographically diverse population (determined using methods such as quota-based sampling) that is representative of the intended user population. Furthermore, the study participants must comprise a diverse range of age and educational levels and have no prior experience with the test or its manufacturer. These factors must be well-defined in the inclusion and exclusion criteria.

(2) All sources of bias (*e.g.,* non-responders) must be predefined and accounted for in the study results with regard to both responders and non-responders.

(3) The testing must follow a format where users have limited time to complete the studies (such as an on-site survey format and a one-time visit with a cap on the maximum amount of time that a participant has to complete the tests).

(4) Users must be randomly assigned to study arms. Test reports in the user comprehension study given to users must define the target condition being tested and related symptoms, explain the intended use and limitations (including warnings) for the test, explain the relevant ethnicities in regard to the variant tested, explain genetic health risks and relevance to the user's ethnicity, and assess participants' ability to understand the following comprehension concepts: the test's limitations, purpose, appropriate action, test results, and other factors that may have an impact on the test results.

(5) Study participants must be untrained, be naïve to the test subject of the study, and be provided the labeling prior to the start of the user comprehension study.

(6) The user comprehension study must meet the predefined primary endpoint criteria, including a minimum of a 90 percent or greater overall comprehension rate (*i.e.,* selection of the correct answer) for each comprehension concept. Other acceptance criteria may be acceptable depending on the concept being tested. Meeting or exceeding this overall comprehension rate demonstrates that the materials presented to the user are adequate for over-the-counter use.

(7) The analysis of the user comprehension results must include:

(i) Results regarding reports that are provided for each gene/variant/ethnicity tested;

(ii) Statistical methods used to analyze all data sets; and

(iii) Completion rate, non-responder rate, and reasons for nonresponse/data exclusion. A summary table of comprehension rates regarding comprehension concepts (*e.g.,* purpose of test, test results, test limitations, ethnicity relevance for the test results, appropriate actions following receipt of results) for each study report must be included.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–16035 Filed 8–20–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2025–N–2424]

Medical Devices; Immunology and Microbiology Devices; Classification of the Mutation Detection Test for Myeloproliferative Neoplasms

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is classifying the mutation detection test for myeloproliferative neoplasms into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for classification of the mutation detection test for myeloproliferative neoplasms. We are taking this action because we

have determined that classifying the device into class II will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices, in part by reducing regulatory burdens.

DATES: This order is effective August 21, 2025. The classification was applicable on March 27, 2017.

FOR FURTHER INFORMATION CONTACT: Ryan Lubert, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3574, Silver Spring, MD 20993–0002, 240–402–6357, *Ryan.Lubert@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the mutation detection test for myeloproliferative neoplasms device as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. In addition, we believe this action will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens by placing the device into a lower device class than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as ''postamendments devices'' because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate device by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through ''De Novo'' classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act (see also part 860, subpart D (21 CFR part 860, subpart D)). Section 207 of the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105–115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112–144) modified the De Novo application process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

We believe this De Novo classification will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens. When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see section 513(f)(2)(B)(i) of the FD&C Act). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application to market a substantially equivalent device (see section 513(i) of the FD&C Act, defining ''substantial equivalence''). Instead, sponsors can use the less burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

On July 1, 2016, FDA received QIAGEN Manchester Ltd.'s request for De Novo classification of the ipsogen JAK2 RGQ PCR Kit. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see section 513(a)(1)(B) of the FD&C Act). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on March 28, 2017, FDA issued an order to the requester classifying the device into class II. In this final order, FDA is codifying the classification of the device by adding 21 CFR 866.6070.[1] We have named the generic type of device ''mutation detection test for myeloproliferative neoplasms,'' and it is identified as 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.

FDA has identified the following risks to health associated specifically with this type of device and the measures required to mitigate these risks in table 1.

TABLE 1—MUTATION DETECTION TEST FOR MYELOPROLIFERATIVE NEOPLASMS RISKS AND MITIGATION MEASURES

Identified risks to health	Mitigation measures
False negative results	Special controls (1) and (2).
False positive results	Special controls (1) and (2).

FDA has determined that special controls, in combination with the general controls, address these risks to

[1] FDA notes that the ''ACTION'' caption for this final order is styled as ''Final amendment; final order,'' rather than ''Final order.'' Beginning in December 2019, this editorial change was made to indicate that the document ''amends'' the Code of Federal Regulations. The change was made in accordance with the Office of Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

health and provide reasonable assurance of safety and effectiveness. For a device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this final order. This device is subject to premarket notification requirements under section 510(k) of the FD&C Act.

III. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Paperwork Reduction Act of 1995

This final order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). The collections of information in part 860, subpart D, regarding De Novo classification have been approved under OMB control number 0910–0844; the collections of information in 21 CFR part 814, subparts A through E, regarding premarket approval have been approved under OMB control number 0910–0231; the collections of information in part 807, subpart E, regarding premarket notification submissions have been approved under OMB control number 0910–0120; the collections of information in 21 CFR part 820 regarding quality system regulation have been approved under OMB control number 0910–0073; and the collections of information in 21 CFR parts 801 and 809 regarding labeling have been approved under OMB control number 0910–0485.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

■ 2. Add § 866.6070 to subpart G to read as follows:

§ 866.6070 Mutation detection test for myeloproliferative neoplasms.

(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). The special controls for this device are:

(1) Design verification and validation must include:

(i) A detailed description of all components in the test, including the following:

(A) A detailed description, including illustrations or photographs of non-standard equipment or methods, of the test components, including all required reagents, instrumentation, and equipment.

(B) Detailed documentation of the device software, including 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.

(ii) 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 study that includes at least two operators per site, two runs per operator per day over a minimum of three 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.

(iii) 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 labeling required under § 809.10(b) of this chapter must include:

(i) An intended use statement, including an indication for use that includes the variant(s)

for which the assay was designed and validated, for example, JAK2 G1849T.

(ii) A detailed description of the performance studies conducted to

comply with paragraph (b)(1)(ii) of this section and a summary of the results.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–16038 Filed 8–20–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2025–N–2108]

Medical Devices; Immunology and Microbiology Devices; Classification of the Anti-Phospholipase A2 Receptor Immunological Test System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is classifying the anti-phospholipase A2 receptor immunological test system into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for the anti-phospholipase A2 receptor immunological test system's classification. We are taking this action because we have determined that classifying the device into class II will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices, in part by reducing regulatory burdens.

DATES: This order is effective August 21, 2025. The classification was applicable on May 29, 2014.

FOR FURTHER INFORMATION CONTACT: Scott McFarland, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3572, Silver Spring, MD 20993–0002, 301–796–6217, *Scott.McFarland@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the anti-phospholipase A2 receptor immunological test system as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. In addition, we believe this action will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens by placing the device into a lower device class than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as ''postamendments devices'' because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate device by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through ''De Novo'' classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act (see also part 860, subpart D (21 CFR part 860, subpart D)). Section 207 of the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105–115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112–144) modified the De Novo application process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

We believe this De Novo classification will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens. When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see section 513(f)(2)(B)(i) of the FD&C Act). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application (PMA) to market a substantially equivalent device (see section 513(i) of the FD&C Act, defining ''substantial equivalence''). Instead, sponsors can use the less burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

For this device, FDA issued an order on March 10, 2014, finding the EUROIMMUN Anti-PLA2R IFA not substantially equivalent to a predicate not subject to PMA. Thus, the device remained in class III in accordance with section 513(f)(1) of the FD&C Act when we issued the order.

On March 28, 2014, FDA received EUROIMMUN US Inc.'s, request for De Novo classification of the EUROIMMUN Anti-PLA2R IFA. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see section 513(a)(1)(B) of the FD&C Act). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on May 29, 2014, FDA issued an order to the requestor classifying the device into class II. In this final order, FDA is codifying the