DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

April 9, 2015

INOVA DIAGNOSTICS, INC.
c/o GABRIELLA LAKOS, MD, PhD
MEDICAL DIRECTOR, DIRECTOR OF ASSAY DEVELOPEMENT
9900 OLD GROVE ROAD
SAN DIEGO, CA 92131

Re: DEN140039
NOVA View® Automated Fluorescence Microscope
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 866.4750
Regulation Name: Automated indirect immunofluorescence microscope and software-assisted system
Regulatory Classification: Class II
Product Code: PIV
Dated: December 11, 2014
Received: December 15, 2014

Dear Dr. Lakos:

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 NOVA View® Automated Fluorescence Microscope, a prescription device. The intended use of the NOVA View® Automated Fluorescence Microscope is

> NOVA View® Automated Fluorescence Microscope is an automated system consisting of a fluorescence microscope and software that acquires, analyzes, stores and displays digital images of stained indirect immunofluorescent slides. It is intended as an aid in the detection and classification of certain antibodies by indirect immunofluorescence technology. The device can only be used with cleared or approved in vitro diagnostic assays that are indicated for use with the device. A trained operator must confirm results generated with the device.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the NOVA View® Automated Fluorescence Microscope, and substantially equivalent devices of this generic type, into class II under the generic name, "Automated indirect immunofluorescence microscope and software-assisted system."

FDA identifies this generic type of device as: Automated indirect immunofluorescence microscope and software-assisted system.

The automated indirect immunofluorescence (IIF) microscope and software-assisted system is a device that acquires, analyzes, stores, and displays digital images of indirect immunofluorescent slides. It is intended to be used as an aid in the determination of antibody status in clinical samples. The device may include a fluorescence microscope with light source, a motorized microscope stage, dedicated instrument controls, a camera, a computer, a sample processor, or other hardware components. The software may include fluorescent signal acquisition and processing software, data storage and transferring mechanisms, or assay specific algorithms to suggest results. A trained operator must confirm results generated with the device.

Section 513(f)(2) of the Food, Drug and 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.

In accordance with section 513(f)(1) and 513(i) of the FD&C Act, FDA issued an order on November 14, 2014, finding the NOVA View® Automated Fluorescence Microscope not substantially equivalent to any device within a type that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or that was subsequently reclassified into class I or class II, which means this device is automatically in class III under section 513(f)(1). On December 15, 2014, FDA received your *de novo* requesting classification of the NOVA View® Automated Fluorescence Microscope into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the NOVA View® Automated Fluorescence Microscope 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 NOVA View® Automated Fluorescence Microscope intended for use as follows:

> NOVA View® Automated Fluorescence Microscope is an automated system consisting of a fluorescence microscope and software that acquires, analyzes, stores and displays digital images of stained indirect immunofluorescent slides. It is intended as an aid in the detection and classification of certain antibodies by indirect immunofluorescence technology. The device can only be used with cleared or approved in vitro diagnostic assays that are indicated for use with the device. A trained operator must confirm results generated with the device.

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 the applicable general controls, provide reasonable assurance of the safety and effectiveness of the device type.

The device (instrument and software system) might be used with a variety of disease indications and associated analytes that must be cleared for use on the device. Risks may vary depending on the indications for use of the specific assay used with the device. The primary risks of this device are related to the consequences of clinical decisions based on false negative and false positive results for a patient due to inaccurate test results or failure to correctly interpret test results. For a false positive result, the risks could include unnecessary testing or inappropriate treatment related to an inaccurate result. For a false negative result, the risk could include a missed or delayed diagnosis. Assay specific performance studies outlined in the special controls will further mitigate risk associated with the device. The identified risks and required mitigations associated with the device type are summarized in the Table below.

Table – Identified Risks to Health and Required Mitigations

Identified Risks to Health	**Required Mitigations**
Inaccurate test results that provide false positive or false negative results.	Special controls (1), (2), and (3)
Failure to correctly interpret test results can lead to false positive or false negative results	Special controls (1), (2)(i), (2)(ii)(A), (2)(ii)(B), (2)(iii), and (3)

In combination with the general controls of the FD&C Act, the automated indirect immunofluorescence microscope and software-assisted system is subject to the following special controls:

(1) The labeling for the device must reference legally marketed assays intended for use with the device.

(2) Premarket notification submissions must include the following information:

(i) A detailed description of the device that includes:
(A) A detailed description of instrumentation and equipment, and illustrations or photographs of non-standard equipment or methods, if applicable.
(B) Detailed documentation of the software, including, but not limited to, standalone software applications and hardware-based devices that incorporate software, if applicable.
(C) A detailed description of appropriate internal and external quality controls that are recommended or provided. The description must identify those control elements that are incorporated into the recommended testing procedures.
(D) Detailed description and specifications for sample preparation, processing

and storage, if applicable.

(E) Methodology and protocols for detecting fluorescence and visualizing results.

(F) Detailed specification of the criteria for test results interpretation and reporting.

(ii) Data demonstrating the performance characteristics of the device, which must include:

(A) A comparison study of the results obtained with the conventional manual method (i.e., reference standard), the device, and the reading of the digital image without aid of the software, using the same set of patient samples for each. The study must use a legally marketed assay intended for use with the device. Patient samples must be from the assay-specific intended use population and differential diagnosis population. Samples must also cover the assay measuring range, if applicable.

(B) Device clinical performance established by comparing device results at multiple U.S. sites to the clinical diagnostic standard used in the U.S., using patient samples from the assay-specific intended use population and the differential diagnosis population. For all samples, the diagnostic clinical criteria and the demographic information must be collected and provided. Clinical validation must be based on the determination of clinical sensitivity and clinical specificity using the test results (e.g., antibody status based on fluorescence to include pattern and titer, if applicable) compared to the clinical diagnosis of the subject from whom the clinical sample was obtained. The data must be summarized in tabular format comparing the result generated by automated, manual, and digital only interpretation to the disease status.

(C) Device precision/reproducibility data generated from within-run, between-run, between-day, between-lot, between-operator, between-instruments, between-site, and total precision for multiple nonconsecutive days (as applicable) using multiple operators, multiple instruments and at multiple sites. A well-characterized panel of patient samples or pools from the associated assay specific intended use population must be used.

(D) Device linearity data generated from patient samples covering the assay measuring range, if applicable.

(E) Device analytical sensitivity data, including limit of blank, limit of detection and limit of quantitation, if applicable.

(F) Device assay specific cut-off, if applicable.

(G) Device analytical specificity data, including interference by endogenous and exogenous substances, if applicable.

(H) Device instrument carryover data, if applicable.

(I) Device stability data including real-time stability under various storage times and temperatures, if applicable.

(J) Information on traceability to a reference material and description of

value assignment of calibrators and controls, if applicable.

(iii) Identification of risk mitigation elements used by the device, including description of all additional procedures, methods, and practices incorporated into the directions for use that mitigate risks associated with testing.

(3) Your 21 CFR 809.10 compliant labeling must include:
- (i) A warning statement that reads "The device is for use by a trained operator in a clinical laboratory setting."
- (ii) A warning statement that reads "All software-aided results must be confirmed by the trained operator."
- (iii) A warning statement that reads "This device is only for use with reagents that are indicated for use with the device."
- (iv) A description of the protocol and performance studies performed in accordance with special control (2)(ii) and a summary of the results, if applicable.

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 automated indirect immunofluorescence microscope and software-assisted system 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 Danielle Turley at 301-796-2851.

Sincerely yours,

Leonthena R. Carrington -A

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