December 11, 2020

Inova Diagnostics, Inc.
Carolina Auza
Supervisor, Research & Development
9900 Old Grove Rd
San Diego, California 92131

Re: K192916
Trade/Device Name: NOVA Lite DAPI dsDNA Crithidia luciliae Kit
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear Antibody Immunological Test System
Regulatory Class: Class II
Product Code: KTL, PIV
Dated: November 11, 2020
Received: November 12, 2020

Dear Carolina Auza:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ying (Katelin) Mao, Ph.D.
Acting Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K192916

Device Name
NOVA Lite DAPI dsDNA Crithidia luciliae Kit

Indications for Use *(Describe)*
NOVA Lite® DAPI dsDNA Crithidia luciliae is an indirect immunofluorescent assay for the qualitative and/or semi-quantitative determination of anti-double stranded DNA (dsDNA) IgG antibodies in human serum by NOVA View Automated Fluorescence Microscope or manual fluorescence microscopy. The presence of anti-dsDNA can be used in conjunction with other serological and clinical findings to aid in the diagnosis of systemic lupus erythematosus (SLE). All results generated with NOVA View device must be confirmed by a trained operator.

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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Table of Contents

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Administrative data

Submitter:
Inova Diagnostics, Inc.
9900 Old Grove Road,
San Diego, CA, 92131

Purpose of submission:
New device(s)

Devices in the submission:
NOVA Lite® DAPI dsDNA *Crithidia luciliae* Kit

Scientific contact:
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Quality Systems contact:
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Phone: 858-586-9900 x 1381
Fax: 858-863-0025
email: relliott@inovadx.com

Device name (assay kit):

Proprietary name:	NOVA Lite® DAPI dsDNA *Crithidia luciliae* Kit
Common name:	anti-double stranded DNA (dsDNA) kit
Classification name:	test system, anti-double stranded DNA (dsDNA) antibodies

Regulation Description:	Antinuclear antibody immunological test system
Regulation Medical Specialty:	Immunology
Review Panel:	Immunology
Product Code:	KTL PIV
Classification Panel:	82- Immunology
Regulation Number:	866.5100- Antinuclear Antibody Immunological Test System
Device Class:	2

Predicate device

NOVA Lite ™ DSDNA, 510(k) number: k880742

Device description

The NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit is an indirect immunofluorescence assay for the qualitative detection and semi-quantitative determination of Anti-dsDNA Antibodies (IgG) in human serum.

Samples are diluted 1:10 in PBS and incubated with the antigen substrate (dsDNA on glass microscope slides). After incubation, unbound antibodies are washed off. The substrate is then incubated with anti-human IgG-FITC conjugate. The conjugate contains a DNA-binding blue fluorescent dye, 4',6-diamidino-2-phenylindole (DAPI) that is required for NOVA View use. The blue dye is not visible by traditional fluorescence microscope at the wavelength where FITC fluorescence is viewed. Unbound reagent is washed off. Stained slides are read by manual fluorescence microscope or scanned with the NOVA View Automated Fluorescence Microscope. The resulting digital images are reviewed and interpreted from the computer monitor. dsDNA positive samples exhibit an apple green fluorescence corresponding to areas of the substrate where autoantibody has bound.

Manual interpretation

A sample is considered positive if specific kinetoplast staining or kinetoplast plus nuclear staining is observed to be greater than the negative control.

NOVA View interpretation

When slides are analyzed by NOVA View, digital images of representative fields of view of the well are captured. These digital images must be reviewed and interpreted from the computer monitor by a trained operator. At the same time when digital images are taken, NOVA View measures the FITC light intensity of the cells that are included in the region. NOVA View reports the measured fluorescence intensity in units of Light Intensity Units (LIU).

NOVA View provides the trained operator with the acquired digital images and the following supportive information:

• LIU value
• Negative/positive/indeterminate classification

NOVA View Single Well Titer (SWT)

The Single Well Titer (SWT) is a software application that estimates the endpoint titer (i.e. the highest dilution that produces positive result) for wells with a positive reaction, based on the obtained LIU.

The NOVA Lite® DAPI dsDNA *Crithidia luciliae* Kit contains the following:

- dsDNA *Crithidia luciliae* Slides; 12 wells/slide, with desiccant
- FITC IgG Conjugate with DAPI, containing 0.09% sodium azide; ready to use.
- Positive Control: dsDNA; human serum with antibodies to dsDNA antigen, containing 0.09% sodium azide; pre-diluted, ready to use.

- Negative Control: IFA System Negative Control, diluted human serum with no dsDNA antibodies present, containing 0.09% sodium azide; pre-diluted, ready to use.
- PBS II (40x) Concentrate, sufficient for making 2000 mL of 1x PBS II.
- Mounting Medium, containing 0.09% sodium azide
- Coverslips

Intended use(s)

NOVA Lite® DAPI dsDNA *Crithidia luciliae* is an indirect immunofluorescent assay for the qualitative and/or semi-quantitative determination of anti-double stranded DNA (dsDNA) IgG antibodies in human serum by NOVA View Automated Fluorescence Microscope or manual fluorescence microscopy. The presence of anti-dsDNA can be used in conjunction with other serological and clinical findings to aid in the diagnosis of systemic lupus erythematosus (SLE). All results generated with NOVA View device must be confirmed by a trained operator.

Indications for use

Same as Intended use.

Substantial equivalence

The NOVA Lite DAPI dsDNA *Crithidia luciliae* reagents have the same intended use and assay principle as the predicate device NOVA Lite ™ DSDNA [510(k) K880742]

Comparison to predicate device

Similarities		
Item	**NOVA Lite DAPI *Crithidia luciliae* Kit**	**Predicate Device**
Intended use	NOVA Lite® DAPI dsDNA *Crithidia luciliae* is an indirect immunofluorescent assay for the qualitative and/or semi-quantitative determination of anti-double stranded DNA (dsDNA) IgG antibodies in human serum by NOVA View Automated Fluorescence Microscope or manual fluorescence microscopy. The presence of anti-dsDNA can be used in conjunction with other serological and clinical findings to aid in the diagnosis of systemic lupus erythematosus (SLE). All results generated with NOVA View device must be confirmed by a trained operator.	NOVA Lite dsDNA Crithidia luciliae is an indirect immunofluorescent assay for the screening and semi-quantitative determination of anti-double stranded DNA (dsDNA) in human serum. The presence of anti-double stranded DNA can be used in conjunction with other serological tests and clinical findings to aid in the diagnosis of systemic lupus erythematosus (SLE).

Similarities		
Item	**NOVA Lite DAPI *Crithidia luciliae* Kit**	**Predicate Device**
Analyte	Anti-dsDNA Antibodies (IgG) in human serum	Anti-dsDNA Antibodies (IgG) in human serum
Assay methodology	indirect immunofluorescence assay	indirect immunofluorescence assay
Antigen	*Crithidia luciliae* cells	*Crithidia luciliae* cells
Sample type	Serum	Serum
Sample dilution	1:10	1:10
Controls	Two levels of controls: one negative, one positive (dsDNA Positive)	Two levels of controls: one negative, one positive (dsDNA Positive)
Storage	2-8 °C	2-8 °C
Shelf life	24 months	24 months

Differences		
Item	**NOVA Lite DAPI *Crithidia luciliae* Kit**	**Predicate Device**
Interpretation	by manual fluorescence microscopy or with the NOVA View device	by manual fluorescence microscopy
Conjugate	FITC conjugated anti-human IgG (Fc specific) with added 4',6-diamidino-2-phenylindole (DAPI)	FITC conjugated anti-human IgG (Fc specific)
Additional dye in Conjugate	4',6-diamidino-2-phenylindole (DAPI)	None

Analytical performance characteristics

Nomenclature used in the studies

All studies have been performed by interpreting the results with both manual microscopy and with the NOVA View system.

- "Manual" and "Manual reading" refers to results obtained by reading the slides with traditional fluorescence microscope.
- "NOVA View" refers to software reported results obtained with the NOVA View Automated Fluorescence Microscope, such as Light Intensity Units (LIU) and positive/negative/indeterminate classification information.
- "Digital", "Digital reading" and "Digital image" refers to results obtained by reading NOVA View generated images on the computer monitor.

For statistical calculations, a positive result is presented as "1", and a negative result is presented as "0". Intensity of the staining is expressed in reactivity grades. Grade 0 is negative; grades 1-4 are weak to strong positive.

4+ Brilliant apple green fluorescence
3+ Bright apple green fluorescence
2+ Clearly distinguishable positive fluorescence
1+ Lowest specific fluorescence that enables the nuclear and/or cytoplasmic staining to be clearly differentiated from the background fluorescence

Precision

To assess the precision performance of the NOVA Lite dsDNA *Crithidia luciliae* Kit results, a study was performed by processing 2 negative, 2 positive and 2 borderline samples with various intensities, in three replicates, in 14 runs (2 runs per day) for 7 days in triplicate resulting in 42 data points for each sample. The slides were read with NOVA view and digital images were interpreted by the operator as well as being read with manual microscope: i.e. three set of results were generated: NOVA view software interpretation, digital image reading results and manual reading results.

Acceptance criteria: Difference between reactivity grades within one run (between replicates) are within ± one reactivity grade. Average reactivity grade difference between any runs is within ± one reactivity grade.

Results: For both digital images reading and manual reading, grades were within ± one reactivity grade within one run (within triplicates), and the average grade was no more than one reactivity grade different between runs.

The results are summarized in the table below.

		Expected Result	**Obtained Result**							
			NOVA View results		**Manual results**			**Digital results**		
Sample	**n**	**Negative/ Positive (grade)**	**% Negative**	**% Positive**	**Grade range (0-4+)**	**% Negative**	**% Positive**	**Grade range (0-4+)**	**% Negative**	**% Positive**
Sample 1	42	Positive (3-4)	7%	93%	3-4	0%	100%	4	0%	100%
Sample 2	42	Negative (0-1)	100%	0%	0-1	98%	2%	0	100%	0%
Sample 3	42	Borderline (0-2)	45%	55%	0-2	14%	86%	1-2	10%	90%
Sample 4	42	Borderline (0-2)	100%	0%	1-2	0%	100%	0-2	69%	31%
Sample 5	42	Positive (1-3)	64%	36%	1-3	0%	100%	1-2	14%	86%
Sample 6	42	Negative (0)	90%	10%	0	100%	0%	0	100%	0%

Reproducibility Studies

Between sites/instruments reproducibility

Ten samples (3 negative, 7 positive) were tested in three replicates, twice a day for 5 days at each site (30 data points per sample). Manual and digital reading was performed by two operators at each site, to assess between operator reproducibility.

Acceptance criteria: 90% agreement between operators and between sites

Grades for site 1:

	Digital Reactivity Grade						**Manual Reactivity Grade**					
	Sample 1						**Sample 1**					
Day	Run 1			Run 2			Run 1			Run 2		
1	4	4	4	4	4	4	3	3	3	4	4	4
2	4	4	4	4	4	4	3	3	3	4	4	4
3	4	4	4	4	4	4	3	3	3	4	4	4
4	4	4	4	4	4	4	4	4	4	3	3	3
5	4	4	4	4	4	4	4	3	4	4	4	4
	Sample 2						**Sample 2**					
1	4	4	4	4	4	4	4	3	3	4	4	4
2	4	4	4	4	4	4	4	4	4	4	4	4
3	4	4	4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4	4	4	4
5	4	4	4	4	4	4	4	4	4	4	4	4
	Sample 3						**Sample 3**					
1	4	4	4	4	4	4	4	4	4	4	4	4
2	4	4	4	4	4	4	4	4	4	4	4	4
3	4	4	4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4	4	4	4
5	4	4	4	4	4	4	4	4	4	4	4	4
	Sample 4						**Sample 4**					
1	3	2	2	2	2	2	2	2	2	2	2	2
2	2	3	3	2	2	2	2	2	2	2	2	2
3	2	3	3	2	2	2	2	2	2	2	2	2
4	2	3	3	2	2	2	2	2	2	2	2	2
5	2	3	3	2	2	2	2	2	2	2	2	2
	Sample 5						**Sample 5**					
1	1	1	1	2	2	2	2	2	2	2	2	2
2	2	2	1	1	1	1	2	2	2	2	2	2
3	2	2	2	2	2	2	2	2	2	2	2	2
4	2	2	2	2	2	2	2	2	2	2	2	2
5	2	2	2	1	1	1	2	2	1	2	2	1
	Sample 6						**Sample 6**					
1	1	1	1	1	1	1	2	2	2	2	2	2
2	1	1	1	1	1	1	1	1	1	2	1	1
3	1	1	1	1	1	1	1	1	1	1	1	1
4	1	1	1	1	1	1	1	1	1	1	1	1
5	1	1	1	1	1	1	1	1	1	1	1	1
	Sample 7						**Sample 7**					
1	4	4	4	4	4	4	3	3	3	3	3	3
2	4	4	4	4	4	4	3	3	3	4	4	4

	Digital Reactivity Grade						**Manual Reactivity Grade**					
3	4	4	4	4	4	4	3	3	3	3	3	3
4	4	4	4	4	4	4	3	3	3	3	3	3
5	4	4	4	4	4	3	3	3	3	3	3	3
	Sample 8						**Sample 8**					
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
	Sample 9						**Sample 9**					
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
	Sample 10						**Sample 10**					
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0

Summary:
Qualitative Agreement (manual reading):

		Expected Results	**Manual Reading**											
			Site1				**Site 2**				**Site 3**			
			Reader 1		**Reader 2**		**Reader 1**		**Reader 2**		**Reader 1**		**Reader 2**	
Sample	**n**	**pos/neg**	**% neg**	**% pos**	**% neg**	**% pos**	**% neg**	**% pos**	**% neg**	**% pos**	**% neg**	**% pos**	**% neg**	**% pos**
1	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
2	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
3	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
4	30	pos	7%	93%	0%	100%	0%	100%	0%	100%	7%	93%	7%	93%
5	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
6	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
7	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
8	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
9	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
10	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%

Qualitative Agreement (digital reading):

		Expected Results	Digital Reading											
			Site1				Site 2				Site 3			
			Reader 1		Reader 2		Reader 1		Reader 2		Reader 1		Reader 2	
Sample	n	pos/neg	% neg	% pos	% neg	% pos	% neg	% pos	% neg	% pos	% neg	% pos	% neg	% pos
1	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
2	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
3	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
4	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
5	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
6	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
7	30	pos	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%
8	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
9	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
10	30	neg	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%

Agreement between reader 1 and reader 2 at each site:

% Overall Agreement (Positive/Negative) between operators (per site)			
	Site 1	Site 2	Site 3
Manual Reading	99.7%	100.0%	100.0%
Digital Reading	100.0%	100.0%	100.0%

Reproducibility between lots

Lot to lot comparison study was performed on two reagent lots. Twenty clinically and/or analytically characterized samples were tested in duplicate.

The following comparisons were made:

- NOVA view output: qualitative agreement.
- Digital image reading: qualitative agreement and grade agreement
- Manual image reading: qualitative agreement and grade agreement comparison.

Acceptance criteria:

- Qualitative positive, negative and total agreement: ≥ 90%
- Grade agreement: ≥ 90% within ± 1 reactivity grade

Qualitative Agreement

Qualitative positive agreements in two-way comparisons ranged from 91.7% to 100.0%

Qualitative negative agreements in two-way comparisons ranged from 96.4% to 100.0%

Qualitative total agreements in two-way comparisons ranged from 95.0%-100.0%

NOVA View Summary Table

NOVA View	Negative agreement (%) (95% CI)	Positive agreement (%) (95% CI)	Total agreement (%) (95% CI)
Lot 046700 vs Lot RP003	96.4 (82.3-99.4)	91.7 (64.6-98.5)	95.0 (83.5-98.6)

Manual Summary Table

NOVA View	Negative agreement (%) (95% CI)	Positive agreement (%) (95% CI)	Total agreement (%) (95% CI)
Lot 046700 vs Lot RP003	100.0 (86.2 – 100.0)	100.0 (80.6– 100.0)	100.0 (91.2 – 100.0)

Digital Summary Table

NOVA View	Negative agreement (%) (95% CI)	Positive agreement (%) (95% CI)	Total agreement (%) (95% CI)
Lot 046700 vs Lot RP003	100.0 (87.1-100.0)	92.9 (68.5-98.7)	97.5 (87.1-99.6)

Grade agreement

All grades (100%) were within ±1 grade from each other for all samples in any pair-wise comparisons for manual and most grades were within ±1 grade from each other for all samples in any pair-wise comparison for digital reading, two comparisons were 100% and one comparison was 98%.

Manual – Agreement +/- 1 reactivity grade = 100%

	RP0003					
046700	**0**	**1**	**2**	**3**	**4**	**Total**
0	24	0	0	0	0	24
1	0	9	0	0	0	9
2	0	0	1	0	0	1
3	0	0	0	4	0	4
4	0	0	0	0	2	2
Total	24	9	1	4	2	40

Digital - Agreement +/- 1 reactivity grade = 98%

	RP0003					
046700	**0**	**1**	**2**	**3**	**4**	**Total**
0	26	0	0	0	0	26
1	1	3	0	0	0	4
2	0	0	2	0	0	2
3	0	0	0	0	0	0
4	0	0	1	1	6	8
Total	27	3	3	1	6	40

Linearity

The linearity study was performed by serially diluting 3 positive samples (one high positive, one medium positive and one low positive) from 1:10 to 1:5120. These samples were assed with the NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit and read with the NOVA View, digital images were interpreted and confirmed. All slides were read with manual microscopy. Qualitative and semi-quantitative results (using a scale of 0 (negative) to 4 (strong positive)) were captured for the manual and digital reading.

Three samples used in the study:

Sample No.	Sample	NOVA View (SWT)	Manual	Digital
1	High Positive	>=320	640	640
2	Medium Positive	40	20	40
3	Low Positive	20	20	20

The sample dilutions and associated intensity grade results are summarized in the table below for manual microscopy:

Sample No.	10	20	40	80	160	320	640	1280	2560	5120
1	4	4	4	4	3	2	1	0	0	0
2	2	2	0	0	0	0	0	0	0	0
3	1	1	0	0	0	0	0	0	0	0

The sample dilutions and associated intensity grades are summarized in the table below for digital reading:

Sample No.	10	20	40	80	160	320	640	1280	2560	5120
1	4	4	4	4	3	2	1	0	0	0
2	2	2	1	0	0	0	0	0	0	0
3	1	1	0	0	0	0	0	0	0	0

Interference

The interference study was performed according to CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition. A set of three specimens were tested (one negative, one positive, one strong positive) using the following Interfering substances (hemoglobin, bilirubin, triglycerides, cholesterol, Rituximab, Methylprednisolone, Cyclophosphamide, Methotrexate, Azathioprine, Ibuprofen, Naproxen, Hydroxychloroquine, Mycophenolate). All interferents were spiked into every specimen at three different concentrations in 10% of total specimen volume, and the resulting samples were assessed in triplicates with the NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit. To assess interference with rheumatoid factor (RF), 10%, 30% and 50% (volume) RF positive sample was added to the test samples. All samples were processed with NOVA Lite DAPI dsDNA *Crithidia luciliae* kit and read with NOVA View. Digital images were interpreted and confirmed. Moreover, all slides were read by the same operator with manual microscopy. Acceptance criteria for the interference studies were grades obtained on samples with interfering substances are within ± 1 reactivity grade of those obtained on the control samples, spiked with diluent. No interference was detected with hemoglobin up to 200 mg/dL, bilirubin up to 100 mg/dL, triglycerides up to 1,000 mg/dL, cholesterol up to 224.3 mg/dL, rheumatoid factor up to 28.02 IU/mL, azathioprine up to 0.03 mg/mL, cyclophosphamide up to 4.1 mg/mL, hydroxychloroquine up to 0.224 mg/mL, ibuprofen up to 5 mg/mL, methotrexate up to 0.1 mg/mL, methylprednisolone up to 0.85 mg/mL, mycophenolate up to 0.004 mg/mL, naproxen up to 5 mg/mL, rituximab up to 7.6 mg/mL, and belimumab up to 8 mg/mL.

Sample Stability and Handling

Three samples, encompassing negative, around the cut-off, and positive samples were tested in duplicates for up to 21 days while stored at 2-8°C, up to 48 hours while stored at room temperature, and after repeated freeze/thaw cycles up to 3 cycles. Results were compared to those obtained on control samples (day zero, stored at 2-8°C).

Acceptance criteria:

- NOVA View results of positive or negative do not change category (positive to negative or negative to positive) and are not different than the control sample.
- Manual reading reactivity grades are within ±1 grade of that of the control sample (stored at 2-8°C)
- Digital image interpretation reactivity grades are within ±1 grade of that of the control sample (stored at 2-8°C).

All samples fulfilled the acceptance criteria at each time point for each condition. Based on these results, we recommend that samples are stored up to 48 hours at room temperature, up to 7 days at 2-8°C and can be subjected to up to 3 freeze/thaw cycles (when samples are stored at or below -20°C).

Reagent Stability

Shelf life

To establish the initial claim for shelf life, accelerated stability studies were performed for up to 4 weeks at 37°C ± 3°C, where one week is equal to six months at 5 ± 3°C.

Accelerated stability testing was performed on all of the components of NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit to support stability claim. The components within the kit are as follows: Slides, conjugate, Negative control, positive control, PBSII and Mounting Medium. Each week a new sealed kit was placed in the incubator, and all components were tested at the end of the experiment together with the one that was stored at 5 ± 3°C. The reactivity of the kits was calculated for each time point (compared to those obtained with 5 ± 3°C stored kit). All calculations were performed by comparing results of the kit stored at 5 ± 3°C (control) to those stored at 37 ± 3°C (test) for 1, 2, 3, and 4 weeks, where one week is equal to six months at 5 ± 3°C. Comparison of reactivity grades between incubated kits against the control kit within the same lot for manual and digital methods.

Acceptance criteria for two-year preliminary expiration dating: Reactivity grades of all samples/reagent controls run must be within ±1 reactivity grade of the control condition (week 0) for both manual and digital image interpretation for all three lots.

The acceptance criteria were successfully met with the accelerated lots tested. All samples tested against those run on the control kit (week 0) were within ±1 reactivity grade of the control kit.

In-use stability

Conjugate

Stability Claim: stable for 8 weeks after opening when stored at 2-8^{o}C given that they have not reached the expiration date found on the label.

During assessing open vial stability, conjugate bottle was opened and then closed and placed in the refrigerator. It was tested each week for 8 weeks against a bottle that was left unopened each week using positive and negative controls on dsDNA *Crithidia luciliae* kits.
Conjugate is considered stable if the following criteria were met:

- Appearance: Clear liquid, free from foreign matter
- The grades from each reading are within ±1 grade from each other.
- Fluorescence grading of >3+ for undiluted positive control and grading of 0 for undiluted negative control.
- Testing is comparable to control

The acceptance criteria were successfully met with all 8 weeks tested.
Controls
Stability Claim: stable for 8 weeks after opening when stored at 2-8^{o}C given that they have not reached the expiration date found on the label.
During assessing open vial stability, control bottles was opened and then closed and placed in the refrigerator. It was tested each week for 8 weeks against a bottle that was left unopened each week using positive and negative controls on dsDNA *Crithidia luciliae* kits.
Conjugate is considered stable if the following criteria were met:

- Appearance: Clear liquid, free from foreign matter
- The grades from each reading are within ±1 grade from each other.
- Fluorescence grading of >3+ for undiluted positive control and grading of 0 for undiluted negative control.
- Testing is comparable to control

The acceptance criteria were successfully met with all 8 weeks tested.

Real time stability
Real time stability testing has been scheduled to be performed each of the time points listed below on the NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit, to verify the 2-year expiration that was assigned based on accelerated stability studies.
At the time of the submission, results were available up to 24 months for lot 1, 15 months for lot 2 and 19 months for lot 3. Complete studies will be done by January 2020.
Acceptance criteria: results should fall within their respective ranges.

All results to date were within the acceptance limits.

Cut-off, reference range
The recommended starting dilution, above which the result is reported as positive and below which the result is reported as negative, is 1:10. The manufacturer suggests performing two-fold dilutions and also recommends that each laboratory establish its own titering protocol.

Clinical performance characteristics

Clinical sensitivity, specificity

To assess clinical performance, a clinical study was performed by Inova Diagnostics on 766 clinically characterized serum samples. The distribution of the cohorts is in the table below:

Diagnosis	N	NOVA View pos		Manual pos		Digital pos	
Systemic Lupus Erythematosus (SLE)	391	223	57%	188	48%	188	48%
Drug Induced Lupus	20	1	5%	1	5%	1	5%
Infectious Disease	60	8	13%	9	15%	8	13%
Vasculitis	30	2	7%	0	0%	0	0%
Primary Antiphospholipid Syndrome	20	5	25%	5	25%	5	25%
Sjogren's Syndrome	30	3	10%	0	0%	0	0%
Celiac Disease	20	1	5%	3	15%	0	0%
Systemic Sclerosis	30	2	7%	3	10%	3	10%
Idiopathic Inflammatory Myopathy	20	4	20%	3	15%	2	10%
Mixed Connective Tissue Disease	20	3	15%	3	15%	3	15%
Crohn's Disease	20	1	5%	1	5%	1	5%
Grave's Disease	20	0	0%	0	0%	0	0%
Hashimoto's Disease	30	6	20%	0	0%	3	10%
Rheumatoid Arthritis	35	2	6%	2	6%	2	6%
Autoimmune Hepatitis (AIH)	20	4	20%	3	15%	1	5%
Total	766	265	35%	221	29%	217	28%

Sensitivity (on SLE) and specificity, calculated on the combined population, are shown below.

N=766	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Manual	48.1 (43.2-53.0)	91.2 (87.9-93.7)
Digital	48.1 (43.2-53.0)	92.3 (89.1-94.6)
NOVA View	57.0 (52.1-61.8)	88.8 (85.2-91.6)

Clinical studies 3 sites

Clinical study was completed at three sites using 269 (clinically characterized samples. All samples were tested on the NOVA Lite DAPI dsDNA (*Crithidia luciliae*) Kit according to its direction insert.

a. Clinical Sensitivity/Specificity:

Sensitivity and specificity for all sites combined (269 x 3 sites= 807 total samples; 100 positive x 3 sites=300; 169 negative x 3 sites= 507)

Correlation to clinical diagnosis for each mode at the three sites

N=807	Clinical Diagnosis	
	Positive/per total SLE	Negative/per total non SLE
NOVA View	120/300	433/507
Manual Reading	98/300	484/507
Digital Reading	102/300	484/507

Summary: clinical overall agreement for all three sites

Performance	NOVA View	Manual Reading	Digital Reading
Sensitivity % (95% CI)	120/300 40.0 (34.6-45.6)	98/300 32.7 (27.6-38.2)	102/300 34.0 (28.9-39.5)
Specificity % (95% CI)	433/507 85.4 (82.1-88.2)	484/507 95.5 (93.3-97.0)	484/507 95.5 (93.3-97.0)

Correlation with SLE clinical diagnosis

Sensitivity (95% CI) N=100	NOVA View	Manual Reading	Digital Reading
Site 1	39/100 39.0 (30.0-48.8)	33/100 33.0 (24.6-42.7)	33/100 33.0 (24.6-42.7)
Site 2	43/100 43.0 (33.7-52.8)	33/100 33.0 (24.6-42.7)	34/100 34.0 (25.5-43.7)
Site 3	38/100 38.0 (29.1-47.8)	32/100 32.0 (23.7-41.7)	35/100 35.0 (26.4-44.7)

Correlation with differential diagnosis

Specificity (95% CI) N=169	NOVA View	Manual Reading	Digital Reading
Site 1	143/169 84.6 (78.4-89.3)	164/169 97.0 (93.3-98.7)	165/169 97.6 (94.1-99.1)
Site 2	143/169 84.6 (78.4-89.3)	159/169 94.1 (89.5-96.8)	161/169 95.3 (90.9-97.6)
Site 3	147/169 87.0 (81.1-91.2)	161/169 95.3 (90.9-97.6)	158/169 93.5 (88.7-96.3)

Summary: sensitivity/specificity, correlation with clinical diagnosis by disease

Disease	N	Site 1			Site 2			Site 3		
		NOVA View	Manual Reading	Digital Reading	NOVA View	Manual Reading	Digital Reading	NOVA View	Manual Reading	Digital Reading
SLE	100	39%	33%	33%	43%	33%	34%	38%	32%	35%
		Specificity Non-SLE								
AIH	20	80%	95%	95%	60%	85%	85%	80%	90%	85%
APS	20	85%	100%	100%	95%	100%	100%	90%	100%	100%
AAV	19	89%	100%	100%	79%	89%	95%	89%	95%	89%
CD	8	100%	100%	100%	88%	100%	100%	88%	100%	100%
CKD	2	100%	100%	100%	0%	100%	100%	100%	100%	100%
COPD	9	78%	89%	100%	89%	100%	100%	100%	100%	100%
CrD	6	100%	100%	100%	100%	100%	100%	100%	100%	100%
HBV	2	100%	100%	100%	50%	100%	100%	100%	100%	100%
HCV	5	100%	100%	100%	80%	100%	100%	100%	100%	100%
HIV	12	100%	100%	100%	100%	100%	100%	100%	100%	100%
RA	20	80%	100%	100%	100%	100%	100%	80%	100%	100%
SjS	20	90%	100%	100%	100%	100%	100%	85%	100%	100%
SSc	20	55%	85%	85%	65%	75%	80%	70%	75%	70%
Syphilis	6	100%	100%	100%	100%	100%	100%	100%	100%	100%

SLE= Systemic Lupus Erytematosus; AIH= Autoimmune Hepatitis; APS= Antiphospholipid Syndrome; AAV= ANCA Associated Vasculitis; CD= Celiac Disease; CKD= Chronic Kidney Disease; COPD= Chronic Obstructive Pulmonary Disease; CrD= Chrohns Disease; HBV= Hepatitis B; HCV= Hepatitis C; HIV= Human Immunodeficiency Virus; RA= Rheumatoid Arthritis; SjS= Sjogren's Syndrome; SSc= Systemic Sclerosis.

Expected values

Expected values were analyzed on 120 samples from apparently healthy subjects: 60 females, 60 males, with mean age of 41 years (range of 18-73).

There were four (3.3%) positive results with manual interpretation and eleven (9.2%) positive results with NOVA View software interpretation and one (0.8%) positive results with digital interpretation with NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit testing.

Comparison with predicate device

Method comparison was performed with results obtained with the NOVA Lite DAPI dsDNA *Crithidia luciliae* Kit by NOVA View software interpretation and with the predicate device was performed using the same 744 serum samples (comprising of 391 serum samples from patients with SLE and 353 samples from patients with other diseases) tested in the clinical study (see table above).

Method comparison results are shown below:

n=744	Positive agreement (%) 95% CI)	Negative agreement (%) 95% CI)	Total agreement (%)
708205 manual vs 708215 manual	87.8 (82.7-91.5)	96.0 (94.0-97.4)	93.7
708205 manual vs 708215 digital	88.0 (82.9-91.7)	94.6 (92.3-96.2)	92.7
708205 manual vs 708215 NOVA View	87.0 (81.8-90.9)	85.3 (82.0-88.0)	85.7

	708205 Manual Grade					
708215 Manual Grade	**0**	**1**	**2**	**3**	**4**	**Total**
0	510	24	1	0	1	536
1	19	34	22	1	0	76
2	2	13	34	4	0	53
3	0	1	6	21	6	34
4	0	2	1	8	34	45
Total	531	74	64	34	41	744

+/- 2 reactivity grade 99.6%

	708205 Manual Grade					
708215 Digital Grade	**0**	**1**	**2**	**3**	**4**	**Total**
0	507	19	5	4	1	536
1	19	15	26	10	6	76
2	5	3	12	24	9	53
3	0	1	1	4	28	34
4	1	0	1	1	42	45
Total	532	38	45	43	86	744

+/- 2 reactivity grade 98.4%

System description

NOVA View Automated Fluorescence Microscope and Software

NOVA View Automated Fluorescence Microscope

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.

The NOVA View device has been cleared by the FDA in DEN140039. Subsequently, the use of NOVA View with ANCA modules has been cleared in k161258. Device description and Principle of Operation were described in DEN140039 and k161258 remained unchanged for this submission.

Software

Level of Concern: Moderate.

The NOVA View software version in this submission contains the following changes compared to the version in k161258:
Addition of CLIFT module and CLIFT SWT application.

When CLIFT slides are analyzed by NOVA View, digital images of representative fields of view of the well are captured. At the same time when digital images are taken, NOVA View measures the FITC light intensity of the cells that are included in the region. NOVA View reports the measured fluorescence intensity in units of Light Intensity Units (LIU).
NOVA View provides the trained operator with the acquired digital images and the following supportive information:
- LIU value
- Negative/positive classification

NOVA View CLIFT Single Well Titer (SWT)
This assay is compatible with NOVA View SWT.

The SWT is a software application that estimates the endpoint titer (e.g., the highest dilution that gives positive result) for wells with a positive reaction with CLIFT, based on the obtained fluorescence intensity. The highest titer that can be differentiated is 1:320. Above this value the NOVA View reports ≥ 320 titer. SWT validation was part of the between sites reproducibility study.

The SWT function was established using 22 dsDNA positive samples that represent various levels of antibodies. Two-fold serial dilutions were made for each sample, starting from 1:10, up to 1:40960. Each dilution was processed on dsDNA *Crithidia luciliae* slides, and the results were interpreted by NOVA View, digital and manual reading. Results were used to establish the intensity curves based on 4-PL logistic curve fitting. NOVA View uses these built-in curves for the determination of the titer

The validation of the SWT function was performed using 31 positive samples. All samples were serially diluted and read using NOVA View and manual microscope (manual end-point titer). SWT was determined for all samples.
Acceptance criteria:

- SWT is within ± 2 dilution steps of that of the manual end-point titer and the digital titer.

Based on 31 samples, 80.6% of SWT results were within ± 1 dilution step of that of the manual titer, and 83.9% were within ±1 dilution step of that of the digital titer, and 93.3% of SWT results were within ± 2 dilution steps of that of the manual titer and 93.5% were within ± 2 dilution steps of that of the digital titer. 2 out of the 31 samples were outside of this range.

SWT, n=31	within ± 1 dilution step	within ± 2 dilution steps
Manual end-point	80.6%	93.5%
Digital end-point	83.9%	93.5%

Additionally, SWT validation was part of the between sites reproducibility study.

Seven positive samples were assayed by all three testing sites (including Inova). 100% (14 out of 14) of SWT results at the two external sites were within ± 1 dilution step of that of the manual titer, and 92.9% (13 out of 14) were within ± 1 dilution step of that of the digital titer; 100% of SWT results were within ± 2 dilution steps of that of both the manual titer and digital titer.