510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K192916

B Applicant

Inova Diagnostics, Inc.

C Proprietary and Established Names

NOVA Lite DAPI dsDNA Crithidia luciliae Kit

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
KTL	Class II	21 CFR 866.5100 - Antinuclear Antibody Immunological Test System	IM - Immunology
PIV	Class II	21 CFR 866.4750 - Automated indirect immunofluorescence microscope and software-assisted system	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New device on a previously cleared instrument

B Measurand:

Anti-double stranded DNA (dsDNA) antibodies

C Type of Test:

Qualitative and semi-quantitative, immunofluorescent assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

This device is only for use with reagents that are indicated for use with the device.
The device is for use by a trained operator in a clinical laboratory setting.
All software-aided results must be confirmed by the trained operator.

D Special Instrument Requirements:

For use only with NOVA View Automated Fluorescence Microscope (DEN140039 and K161258).

IV Device/System Characteristics:

A Device Description:

NOVA Lite® DAPI dsDNA Crithidia luciliae Kit is an indirect immunofluorescence assay for the qualitative detection and semi-quantitative determination of anti-double stranded DNA (dsDNA) of IgG isotype in human serum.

Assay kit components include:

- 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

Materials needed but not provided:

NOVA View Automated Fluorescence Microscope cleared by FDA in DEN140039 and K161258.

B Principle of Operation:

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 (FI) 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):
NOVA Lite dsDNA

B Predicate 510(k) Number(s):
K880742

C Comparison with Predicate(s):

Item	Candidate (K192916)	Predicate (K880742)
Device Trade Name	NOVA Lite DAPI dsDNA Crithidia luciliae Kit	NOVA Lite dsDNA
General Device Characteristic Similarities		
Intended Use / Indications For Use	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.	An indirect immunofluorescent test system for screening and semi-quantitative determination of Anti double-stranded (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).
Analyte	Anti-dsDNA Antibodies (IgG) in human serum	Anti-dsDNA Antibodies (IgG) in human serum
Assay methodology	Indirect immunofluorescence assay	Same
Manual Interpretation	Manual fluorescence microscopy	Same
Antigen	*Crithidia luciliae* cells	Same
Sample Matrix	Serum	Same
Sample dilution	1:10	Same
Controls	Two levels of controls: one negative, one positive (dsDNA Positive)	Same
Storage	2-8^{o}C	Same
Shelf life	24 months	Same

Item	Candidate (K192916)	Predicate (K880742)
Device Trade Name	NOVA Lite DAPI dsDNA Crithidia luciliae Kit	NOVA Lite dsDNA

General Device Characteristic Differences		
Interpretation	NOVA View Automated Fluorescence Microscope	Manual only
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

VI Standards/Guidance Documents Referenced:

- CLSI EP12-A2, 2nd Edition, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline
- CLSI EP07-A2, 2nd Edition: Interference Testing in Clinical Chemistry

VII Performance Characteristics (if/when applicable):

Nomenclature used in the studies:

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

- Manual method: Manual and "Manual reading" refers to results obtained by reading the slides with traditional fluorescence microscope.

- NOVA View method: "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 Method: "Digital", "Digital reading" and "Digital image" refers to results obtained by reading NOVA View generated images on the computer monitor.

b) For statistical calculations, a positive result is presented as "1", and a negative result is presented as "0". The fluorescence intensity (FI) of the staining is expressed in reactivity grades. Grade 0 is negative; grades 1–4 are weak to strong positive.

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

For all studies presented here, all results met the sponsor's pre-determined acceptance criteria.

A Analytical Performance:

1. Precision/Reproducibility:

a) *Within-Lab Precision*: A study was performed by processing six samples (two negative, two positive and two borderline samples) with various intensities, in three replicates, in 14 runs (two runs per day) for seven days resulting in 42 data points (N) for each sample. The slides were read by the three methods described above (Manual, NOVA View and Digital) and three sets of results were generated, including manual reading results, NOVA View software interpretation, digital image/monitor reading 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		Manual results			Digital results		
Sample	n	neg/pos (grade)	% neg	% pos	** Grade	% neg	% pos	** Grade	% neg	% pos
1	42	Positive (3-4)	7%	93%	3-4	0%	100.0%	4	0%	100%
2	42	Negative (0-1)	100%	0%	0-1	98%	2.4%	0	100%	0%
3	42	Borderline (0-2)	45%	55%	0-2	14%	85.7%	1-2	10%	90%
4	42	Borderline (0-2)	100%	0%	1-2	0%	100.0%	0-2	69%	31%
5	42	Positive (1-3)	64%	36%	1-3	0%	100.0%	1-2	14%	86%
6	42	Negative (0)	90%	10%	0	100%	0.0%	0	100%	0%

pos = Positive
neg = Negative
NOVA* = NOVA View Automated Fluorescence Microscope results
Grade** = Grade Range (0-4+)

b) *Between sites/instruments reproducibility*: Ten samples, including three negative and seven positive (representing the intensity range across four positive grades), were tested in three replicates, twice a day for five 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.

		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

pos = Positive
neg = Negative

Qualitative Agreement (digital reading):

Sample	n	Expected Results	Digital Reading											
			Site1				Site 2				Site 3			
			Reader 1		Reader 2		Reader 1		Reader 2		Reader 1		Reader 2	
		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

pos = Positive
neg = Negative

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%

c) *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

Qualitative Agreement: Qualitative total agreements in two-way comparisons ranged from 95.0% to 100.0%.

Lot-to-lot comparison	Negative agreement (%) (95% CI)	Positive agreement (%) (95% CI)	Total agreement (%) (95% CI)
NOVA View	96.4 (82.3–99.4)	91.7 (64.6–98.5)	95.0 (83.5–98.6)
Manual	100.0 (86.2–100.0)	100.0 (80.6–100.0)	100.0 (91.2–100.0)
Digital	100.0 (87.1–100.0)	92.9 (68.5–98.7)	97.5 (87.1–99.6)

Grade agreement:

Grades 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%

	Lot-2					
Lot-1	0	1	2	3	4	Total
0	24	0	0	0	0	24
1	0	7	0	0	0	7
2	0	2	1	0	0	3
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%

	Lot-2					
Lot-1	0	1	2	3	4	Total
0	26	1	0	0	0	27
1	0	3	0	0	0	3
2	0	0	2	0	0	2
3	0	0	0	0	0	0
4	0	0	0	0	8	8
Total	26	4	2	0	8	40

2. Linearity:

The linearity study was performed by serially diluting three positive samples (one high positive, one medium positive and one low positive) from 1:10 to 1:5,120. These samples were assessed 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.

Samples used in the study

Sample #	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 #	10	20	40	80	160	320	640	1,280	2,560	5,120
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 #	10	20	40	80	160	320	640	1,280	2,560	5,120
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

3. Analytical Specificity/Interference:

a) *Interference studies*: The interference study was performed according to CLSI EP07-A2 (*Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition, November 2005*) to determine the effect of various endogenous and exogenous substances on the NOVA Lite DAPI dsDNA Crithidia luciliae assay. A set of three specimens were tested (one negative, one positive, one strong positive) using interfering substances.

i) *Endogenous Substance Interference*: Endogenous interfering substances including hemoglobin, bilirubin, triglycerides/cholesterol were tested at concentrations shown in the table below. To assess interference with rheumatoid factor (RF), 10%, 30% and 50% (volume) RF positive sample was added to the test samples.

Interfering Substance	Final Concentration tested		
	Maximum	Medium	Minimum
Hemoglobin	200 mg/dL	100 mg/dL	50 mg/dL
Bilirubin	100 mg/dL	50 mg/dL	25 mg/dL
Triglycerides	1,000 mg/dL	500 mg/dL	250 mg/dL
Cholesterol	224.3 mg/dL	112.1 mg/dL	56.1 mg/dL
RF IgM	56.04 IU/mL	39.23 IU/mL	28.02 IU/mL

ii) *Exogenous Substance Interference*: Exogenous interfering substances including rituximab, methylprednisolone, cyclophosphamide, methotrexate, azathioprine, ibuprofen, naproxen, hydroxychloroquine and mycophenolate were tested at concentrations shown in the table below.

Interfering Substance	Final Concentration tested		
	Maximum	Medium	Minimum
Rituximab	7.6 mg/mL	3.8 mg/mL	1.9 mg/mL
Methylprednisolone	0.85 mg/mL	0.43 mg/mL	0.213 mg/mL
Cyclophosphamide	4.1 mg/mL	2.05 mg/mL	1.025 mg/mL

Methotrexate	0.01 mg/mL	0.005 mg/mL	0.0025 mg/mL
Azathioprine	0.03 mg/mL	0.015 mg/mL	0.0075 mg/mL
Ibuprofen	5 mg/mL	2.5 mg/mL	1.25 mg/mL
Naproxen	5 mg/mL	2.5 mg/mL	1.25 mg/mL
Hydroxychloroquine	0.224 mg/mL	0.112 mg/mL	0.056 mg/mL
Mycophenolate	0.004 mg/mL	0.002 mg/mL	0.001 mg/mL
Belimumab	8 mg/mL	4 mg/mL	2 mg/mL

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. 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.

No interference was detected with the tested substances, up to the maximal concentrations indicated in tables above.

b) *Cross-reactivity*:

The specificity of the NOVA Lite DAPI dsDNA Crithidia luciliae kit was verified using the ANA reference panel obtained from the Centers for Disease Control and Prevention, Atlanta, USA (12 samples). CDC sample (#1) specific for DNA was positive by NOVA View, digital and manual reading with an intensity grade of +4. All the remaining samples tested were negative on NOVA View, digital and manual modes with the exception of sample #7 being a weak positive (+1) for NOVA View and digital reading modes.

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a) *Traceability*: A recognized standard or reference material for anti-dsDNA antibodies is not available.

b) *Kit Stability*:

Accelerated stability studies were performed for up to 4 weeks at 37°C ± 3°C. The testing was performed using positive control, negative control and patient panel on all the components of NOVA Lite DAPI dsDNA Crithidia luciliae Kit including, slides, conjugate, negative control, positive control, PBSII and mounting medium. 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.

The stability data support 8 weeks shelf-life for the FITC IgG Conjugate with DAPI, dsDNA Positive and IFA System Negative Control after opening when stored at 2–8ºC.

c) *Sample Stability*:

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).

Based on the results, the stability data support sample storage up to 48 hours at room temperature, up to 7 days at 2-8°C and up to 3 freeze/thaw cycles (when samples are stored at or below -20°C).

6. Detection Limit:

Not applicable

7. Assay Cut-Off:

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 recommends that each laboratory establish its own titering protocol.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The method comparison study was performed using 744 serum samples, including 391 serum samples from patients with SLE and 353 samples from patients with other diseases (the composition of the cohort is described in the "Clinical Studies" section below). The results obtained with the NOVA Lite DAPI dsDNA Crithidia luciliae Kit by NOVA View software interpretation and with the predicate device are shown below:

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

Grade agreement: Comparison of the grade assignments for the candidate device to that of the predicate device (as shown in the tables below) for manual reads were 99.6% within +/- 2 reactivity grade, and for digital reads were 98.4% within +/- 2 reactivity grade.

Candidate Manual Grade	Predicate 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

Candidate Digital Grade	Predicate Manual 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. Matrix Comparison:

   Not applicable

C Clinical Studies:

1. *Clinical Sensitivity and Specificity*:

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

Diagnosis	N	NOVA View positive		Manual positive		Digital positive	
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.

	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 at three sites:

Additionally, 269 clinically characterized serum samples were tested at a sponsor lab (Site 1) and at two external clinical sites (Site 2 and Site 3). 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) is shown below:

Clinical diagnosis overall agreement for all three sites:

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

Correlation with SLE clinical diagnosis at each site:

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

Correlation with differential diagnosis at each site:

	N=169, Specificity % (95% CI)		
	NOVA View	Manual Reading	Digital Reading
Site 1	84.6% (143/169) (78.4–89.3%)	97.0% (164/169) (93.3–98.7%)	97.6% (165/169) (94.1–99.1%)
Site 2	84.6% (143/169) (78.4–89.3%)	94.1% (159/169) (89.5–96.8%)	95.3% (161/169) (90.9–97.6%)

Site 3	87.0% (147/169) (81.1–91.2%)	95.3% (161/169) (90.9–97.6%)	93.5% (158/169) (88.7–96.3%)

Sensitivity/specificity, correlation with clinical diagnosis by disease:

		Site 1			Site 2			Site 3		
Disease	N	NOVA View	Manual Read	Digital Read	NOVA View	Manual Read	Digital Read	NOVA View	Manual Read	Digital Read
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%

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

2. Other Clinical Supportive Data:

Not applicable.

D Clinical Cut-Off:

See assay cut-off

E Expected Values/Reference Range:

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.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.