5. 510(K) SUMMARY

5.1. Submitter

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5.2. Submission Contact

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5.3. Date Prepared

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5.4. Proprietary and Established Names

Sofia 2 Lyme FIA
Sofia Lyme Control Set

5.5. Common Name

Lyme IgG and Lyme IgM test and assayed external controls

5.6. Regulatory Information

Product Code	Classification	Regulatory Section	Panel
LSR	II	21 CFR 866.3830	Immunology and Microbiology Devices

5.7. Predicate Device

Vidas Lyme IgG and Vidas Lyme IgM

5.8. Device Description

The Sofia 2 Lyme FIA is an immunofluorescence-based, lateral flow assay for detection of IgM and/or IgG antibodies to *Borrelia burgdorferi* in patient specimens. Reagents for the assay are ready-to-use and provided in the kit.

The assay uses a bidirectional test strip format to detect both IgM and IgG antibodies to *B. burgdorferi*. One side of the test strip detects IgM antibodies to *B. burgdorferi* and the other side of the test strip detects IgG antibodies to *B. burgdorferi*.

To perform the test, the patient finger-stick whole blood specimen is obtained with the provided Capillary Tube (a.k.a. whole blood separator device). The Capillary Tube stands or is held vertically to allow the blood to drain. This device separates the red blood cells from the whole blood specimen using a gravimetric flow through a sample pad coated with rabbit anti-human red blood cell (RBC) antibodies. The user dispenses all of the Reagent Solution into the Reagent Tube and inserts the Capillary Tube into the Reagent Tube and shakes the tube vigorously. Two drops of diluted sample are dispensed into the round sample well located near the center of the Test Cassette.

The Test Cassette is loaded into Sofia 2 in either the READ NOW Mode or WALK AWAY Mode. In READ NOW Mode, the user allows the cassette to develop on the countertop for 15 minutes. In WALK AWAY Mode, the user immediately after adding the specimen to the cassette, the cassette is inserted into Sofia 2. Sofia 2 will analyze the test strip at 3, 5, 8, 10, and 15 minutes until both IgM and IgG positive results are received. This feature allows for earlier read times.

Each Sofia 2 Lyme FIA kit will contain one Positive and one Negative Control—each provided in separate dropper bottles. The external controls will be provided separately as well in a Sofia Lyme Control Set. The Positive and Negative QC controls are formulated with patient Lyme IgM and IgG positive serum that are diluted into 1X PBS and 0.3% Microcide is added to the solution as an antimicrobial. The External Controls will be tested by adding 2 drops to the test cassette.

5.9. Intended Use

Intended Use Statements for Sofia 2 Lyme FIA and Sofia Lyme Control Set:

Sofia 2 Lyme FIA:
The Sofia 2 Lyme FIA employs immunofluorescence for the rapid differential detection of human IgM and IgG antibodies to *Borrelia burgdorferi* from finger-stick whole blood specimens from patients suspected of *B. burgdorferi* infection of at least 2 weeks' duration. The Sofia 2 Lyme FIA is intended for use as an aid in diagnosis of Lyme disease. A negative result does not preclude infection with *B. burgdorferi*. Positive results must be confirmed by testing with a corresponding second-tier *B. burgdorferi* Western blot assay. Test results are to be used in conjunction with information obtained from the patient's clinical evaluation and other diagnostic procedures. The assay is to be performed on the Sofia 2 instrument. Professional guidelines should be consulted regarding testing and treatment for Lyme disease when acute *B. burgdorferi* infection is suspected.

Sofia Lyme Control Set:
The Sofia Lyme Control Set is intended for use as assayed quality control materials to verify the performance of the Sofia Lyme FIA and Sofia 2 Lyme FIA test system.

5.10. Substantial Equivalence Information:

1. Predicate Device Name: Vidas Lyme IgM and Vidas Lyme IgG

2. Predicate 510(k) Numbers: K122979 and K122986

Comparison with Predicate

Item	Proposed Device	Predicate IgM Device	Predicate IgG Device
Features	**Sofia 2 Lyme FIA with Sofia**	**Biomerieux Vidas Lyme IgM**	**Biomerieux Vidas Lyme IgG**
Intended Use	Sofia 2 Lyme FIA: The Sofia 2 Lyme FIA employs immunofluorescence for the rapid differential detection of human IgM and IgG antibodies to *Borrelia burgdorferi* from finger-stick whole blood specimens from patients suspected of *B. burgdorferi* infection of at least 2 weeks' duration. The Sofia 2 Lyme FIA is intended for use as an aid in diagnosis of Lyme disease. A negative result does not preclude infection with *B. burgdorferi*. Positive results must be confirmed by testing with a corresponding second-tier *B. burgdorferi* Western blot assay. Test results are to be used in conjunction with information obtained from the patient's clinical evaluation and other diagnostic procedures. The assay is to be performed on the Sofia 2 instrument. Professional guidelines should be consulted regarding testing and	The VIDAS Lyme IgM assay is an automated qualitative enzyme immunoassay intended for use on the instruments of the VIDAS family in the presumptive detection of human IgG antibodies to *Borrelia burdorferi* in human serum or plasma. It should be used to test patients with a history and/or symptoms of infection with *B. burgdorferi*. All VIDAS Lyme IgG positive specimens should be further tested with a Western Blot IgG assay to obtain supportive evidence of infection with *B. burgdorferi*.	The VIDAS Lyme IgG assay is an automated qualitative enzyme immunoassay intended for use on the instruments of the VIDAS family in the presumptive detection of human IgG antibodies to *Borrelia burdorferi* in human serum or plasma. It should be used to test patients with a history and/or symptoms of infection with *B. burgdorferi*. All VIDAS Lyme IgG positive specimens should be further tested with a Western Blot IgG assay to obtain supportive evidence of infection with *B. burgdorferi*.

Item	Proposed Device	Predicate IgM Device	Predicate IgG Device
Features	**Sofia 2 Lyme FIA with Sofia**	**Biomerieux Vidas Lyme IgM**	**Biomerieux Vidas Lyme IgG**
	treatment for Lyme disease when acute *B. burgdorferi* infection is suspected. Sofia Lyme Control Set: The Sofia Lyme Control Set is intended for use as assayed quality control materials to verify the performance of the Sofia Lyme FIA and Sofia 2 Lyme FIA test system.		
Instrument	Sofia 2	VIDAS and miniVIDAS	VIDAS and miniVIDAS
Analyte	Human IgM and IgG antibodies against *B. burgdorferi* proteins	Human IgM antibodies against *B. burgdorferi* proteins	Human IgG antibodies against *B. burgdorferi* proteins
Automated Analysis	Yes	Yes	Yes
Read Results	Read results on instrument screen or print with optional printer	Result report is printed	Result report is printed
Read Result Time	Potential for early read in Walk-Away Mode. Sofia 2 will image cassette at 3, 5, 8, 10, and 15 minutes until both IgM and IgG positive results are received.	27 minutes	27 minutes
Specimen Types	Finger-stick whole blood	Serum and plasma	Serum and plasma
Qualitative	Yes	Yes	Yes
Test Principle	Immunofluorescence Device	Immunofluorescence Device	Immunofluorescence Device
Format	Lateral-flow Bi-directional Test Cassette	Enzyme-linked fluorescent assay (ELFA)	Enzyme-linked fluorescent assay (ELFA)
Antibodies Used	Monoclonal anti-human IgG and polyclonal anti-human IgM	Anti-human IgM antibodies	Anti-human IgG antibodies

Item	Proposed Device	Predicate IgM Device	Predicate IgG Device
Features	**Sofia 2 Lyme FIA with Sofia**	**Biomerieux Vidas Lyme IgM**	**Biomerieux Vidas Lyme IgG**
Antigens Used	Recombinant Proteins and synthetic peptides of *B. burgdorferi*	Recombinant proteins of *B. burgdorferi*	Recombinant proteins of *B. burgdorferi*
Detection Method	Polystyrene microparticles dyed with Europium chelate	Alkaline phosphatase/4-MUP	Alkaline phosphatase/4-MUP
Storage	Room Temperature (15-30°C)	2-8°C	2-8°C
Running Buffer Solution	One pre-filled vial containing PBS	Sample diluent and wash buffer	Sample diluent and wash buffer
Quality Control Features	Built-in features include: • Built-in procedural control zone scanned by the analyzer to determine whether adequate flow occurred on the IgG side of the assay. • Built-in reference control line scanned by the analyzer to determine whether adequate flow occurred on the IgM side of the assay. • Analyzer prevents used or expired cartridge from being read by the reader • Cassette must be properly inserted	• One positive and one negative control are included and must be tested after opening a new kit to monitor reagent failure.	• One positive and one negative control are included and must be tested after opening a new kit to monitor reagent failure.

5.11. Performance Data

Studies were undertaken to document the performance characteristics of Sofia 2 Lyme FIA and the Sofia Lyme Control Set, as well as to compare the performance between Sofia 2 Lyme and the Vidas IgG and IgM tests. The studies included the following:

ANALYTICAL STUDIES

a. Precision

The precision of the Sofia Lyme FIA with Sofia 2 was evaluated at one Quidel site utilizing 2 operators and 2 Sofia 2 instruments. Contrived samples were prepared at levels that ranged from negative to moderate positive for both IgM and IgG. Each sample was tested by 2 operators in duplicate with a total of 24 different runs (2 runs per day over a total of 12 days) for a total of 96 times over the course of the study.

Sofia Lyme FIA with Sofia 2 Precision – Within Run

IgM or IgG Sample	IgM Positive		IgM % Positivity	IgG Positive		IgG % Positivity
	Run 1	Run 2	Total (n=96)	Run 1	Run 2	Total (n=96)
Negative	0/48	0/48	0%	0/48	0/48	0%
High Negative (C_5)	0/48	0/48	0%	0/48	0/48	0%
Low Positive (C_{95})	48/48	48/48	100%	48/48	46/48	100%
Moderate Positive (2-3X)	48/48	48/48	100%	48/48	48/48	100%

Sofia Lyme FIA with Sofia 2 Precision – Between Operator

IgM or IgG Sample	IgM Positive		IgM % Positivity	IgG Positive		IgG % Positivity
	Operator 1	Operator 2	Total (n=96)	Operator 1	Operator 2	Total (n=96)
Negative	0/48	0/48	0%	0/48	0/48	0%
High Negative (C_5)	0/48	0/48	0%	0/48	0/48	0%
Low Positive (C_{95})	48/48	48/48	100%	48/48	48/48	100%
Moderate Positive (2-3X)	48/48	48/48	100%	48/48	48/48	100%

b. Reproducibility

This study demonstrated intra- and inter-laboratory reproducibility with a panel of test samples at various concentrations of IgM and IgG antibodies to *B. burgdorferi*. The operators and laboratories obtained accurate results with the Sofia Lyme FIA on Sofia 2.

Sofia Lyme FIA with Sofia 2 Reproducibility Study Inter-Laboratory Agreement

Site	IgM Negative (C_0)	IgM High Negative (C_5)	IgM Low Positive (C_{95})	IgM Moderate Positive (2-3X LOD)	IgG Negative (C_0)	IgG High Negative (C_5)	IgG Low Positive (C_{95})	IgG Moderate Positive (2-3X LOD)
1	30/30	30/30	30/30	30/30	30/30	30/30	30/30	30/30
2	30/30	30/30	30/30	30/30	30/30	30/30	30/30	30/30
3	30/30	30/30	27/30	28/30	30/30	30/30	25/30	30/30
Total	**90/90**	**90/90**	**87/90**	**88/90**	**90/90**	**90/90**	**85/90**	**90/90**
% Overall Agreement (95% CI)	**100% (95.1-100%)**	**100% (95.1-100%)**	**96.7% (90.3-99.3%)**	**97.8% (91.8-99.9%)**	**100% (95.1-100%)**	**100% (95.1-100%)**	**94.4% (87.3-97.9%)**	**100% (95.1-100%)**

c. Assay Cutoff

An Assay Cutoff Study was performed to determine and confirm the two separate assay cutoff limits for the Sofia 2 Lyme FIA. One cutoff limit was established for Lyme IgG and one cutoff limit was established for Lyme IgM. The general procedure was to test matched finger-stick whole blood, serum and plasma samples with the aim of setting the whole blood assay cutoff so that the clinical performance, percent positive agreement (PPA) and the percent negative agreement (NPA), of the whole blood assay is statistically similar to the FDA cleared Sofia Lyme FIA serum and plasma assay. After the cutoffs were established, the values were validated as part of the clinical trial as well as other analytical studies

d. Interference Substances

A study was performed to assess potential interfering substances with the Sofia Lyme FIA with Sofia. There was no interference or cross-reactivity results when tested with the Sofia Lyme FIA.

Sofia Lyme FIA with Sofia Interfering Substances

Interfering Substance	Concentrations Tested
Bilirubin	15 mg/dL
Hemoglobin	20 g/dL
Lipids	750 mg/dL
Albumin	5.0 g/dL
Acetylsalicylic Acid	3.62 mmol/L
Amoxicillin	206 µmol/L
Azithromycin	15.3 µmol/L
Ceftriaxone	1460 µmol/L
Cefuroxime Axetil	1416 µmol/L
Doxycycline Hyclate	67.5 µmol/L
Erythromycin	81.6 µmol/L
Ibuprofen	2425 µmol/L
Minocycline	10.33 µmol/L
Penicillin G	33.67 µmol/L
Penicillin Phenoxymethyl	14.27 µmol/L
Prednisolone	8.31 µmol/L
Tetracyclines	34 µmol/L

e. Cross Reactivity

The cross-reactivity of the Sofia Lyme FIA with Sofia was evaluated with 17 disease state sample types that have the potential to interfere.

Sofia Lyme FIA with Sofia Cross-Reactivity

Disease State Diagnosis	# of Samples	IgM Positive Results	IgG Positive Results
Anti-Nuclear Antibodies	10	4/10	1/10
Babesiosis	12	3/12	4/12
Chronic Fatigue Syndrome	12	2/12	2/12
Cytomegalovirus	11	2/11	1/11
Epstein Barr Virus	10	4/10	0/10
Fibromyalgia	10	1/10	0/10
H. pylori	10	4/10	0/10
HIV	11	2/11	0/11
Influenza	11	0/11	0/11
Leptospirosis	6	1/6	2/6
Lupus	20	8/20	4/20
Multiple Sclerosis	10	1/10	1/10
Parvovirus B19	15	4/15	1/15
Rheumatoid Factor	10	0/10	0/10
Rickettsia	3	0/3	0/3
Rocky Mountain Spotted Fever	10	0/10	0/10
Syphilis	28	8/28	4/28

Note: The results obtained with Leptospirosis (6) and Rickettsia (3) samples may not be conclusive due to low number of samples tested. See also the Limitations section.

CLINICAL STUDIES

f. Matrix Equivalency

The finger-stick whole blood matrix on the Sofia 2 Lyme FIA was demonstrated to be equivalent to the serum/plasma matrix on the Sofia Lyme FIA. A field study was conducted using matched finger-stick whole blood, serum and plasma.

Matrix Equivalency

n=321	IgM			IgG		
	Finger-stick Whole Blood	**Serum**	**Plasma**	**Finger-stick Whole Blood**	**Serum**	**Plasma**
Positive	136	135	133	105	96	98
Negative	185	186	188	216	225	223
% Positivity	**42.4%**	**42.1%**	**41.4%**	**32.7%**	**29.9%**	**30.5%**

g. CDC Reference Panel

When testing the CDC reference panel, the overall agreement for Clinical Status of IgG and IgM samples between Sofia Lyme FIA and Clinical Status and Western Blot was good.

Sofia Lyme FIA with Sofia tested with CDC Panel – IgM Results

Clinical Status		**Sofia Lyme IgM**			**Western Blot Lyme IgM**		
	n	Pos	Neg	% Agreement with clinical Status	Pos	Neg	% Agreement with clinical Status
Negative Controls	190	33	157	82.6%	0	190	100.0%
Early Lyme EM Positive	60	49	11	81.7%	31	29	51.7%
Late Lyme	30	22	8	73.3%	17	13	56.7%

Sofia Lyme FIA with Sofia tested with CDC Panel – IgG Results

Clinical Status		**Sofia Lyme IgG**			**Western Blot Lyme IgG**		
	n	Pos	Neg	% Agreement with clinical Status	Pos	Neg	% Agreement with clinical Status
Negative Controls	190	25	165	86.8%	0	190	100.0%
Early Lyme EM Positive	60	49	11	81.7%	19	41	31.7%
Late Lyme	30	30	0	100%	26	4	86.7%

h. Specificity Study

This study evaluated the analytical specificity of the Sofia Lyme FIA on Sofia 2 using samples obtained from asymptomatic (healthy, normal) populations in both endemic and non-endemic regions. The overall specificity of the Sofia Lyme FIA was very good.

Sofia Lyme FIA with Sofia 2 and Predicate Analytical Specificity

	n	Sofia IgM	Predicate IgM*		Sofia IgG	Predicate IgG
Endemic	100	86.0%	80.0%		95.0%	98.0%
Non-Endemic	100	93.0%	93.0%		98.0%	99.0%
Total	**200**	**89.5%**	**86.5%**		**96.5%**	**98.5%**

*Equivocal results were considered Positive.

i. Sensitivity Study

This study evaluated the clinical sensitivity of the Sofia Lyme FIA device using well-characterized clinically or culture confirmed Lyme disease samples. The clinical sensitivity was compared to a 510(k) cleared test and the performance was comparable.

Lyme IgM Results for Sofia Lyme FIA with Sofia Compared to Predicate Assay

		Sofia IgM				Predicate IgM				
Category	**n**	**Pos**	**Neg**	**Sens**	**95% CI**	**Pos**	**Equiv**	**Neg**	**Sens[1]**	**95% CI**
Acute, < 1 month, with EM	**64**	39	25	60.9%	48.7-72.0%	28	8	28	56.3%	44.1-67.7%
Acute, 1-2 months, with EM	**4**	3	1	75.0%	28.9-96.6%	2	0	2	50.0%	15.0-85.0%
Convalescent, 3-12 months, with EM	**15**	11	4	73.3%	47.6-89.5%	6	2	7	53.3%	30.1-75.2%
Late Lyme (>1 yr), Neuro or Arthritic	**12**	8	4	66.7%	38.8-86.5%	7	3	2	83.3%	54.0-96.5%
All Categories	**95**	61	34	64.2%	54.2-73.1%	43	13	39	58.9%	48.9-68.3%

[1]Of the 13 samples that were "equivocal" by the predicate, 12 of 13 were negative by FDA approved western blot.

Lyme IgG Results for Sofia Lyme FIA with Sofia Compared to Predicate Assay

		Sofia IgG				Predicate IgG			
Category	**n**	**Pos**	**Neg**	**Sens**	**95%CI**	**Pos**	**Neg**	**Sens**	**95%CI**
Acute, < 1 month, with EM	**64**	50	14	78.1%	66.5-86.6%	28	36	43.8%	32.3-55.9%
Acute, 1-2 months, with EM	**4**	4	0	100%	54.3-100.0%	3	1	75.0%	28.9-96.6%
Convalescent, 3-12 months, with EM	**15**	10	5	66.7%	41.5-85.0%	6	9	40.0%	19.8-64.3%
Late Lyme (>1 yr), Neuro or Arthritic	**12**	12	0	100%	78.4-100.0%	10	2	83.3%	54.0-96.5%
All Categories	**95**	76	19	80.0%	70.8-86.9%	47	48	49.5%	39.6-59.4%

j. Method Comparison

This study demonstrated that Sofia 2 Lyme FIA with Sofia 2 has comparable performance to the Vidas Lyme IgG and Vidas Lyme IgM tests when testing prospectively collected specimens from subjects suspected of having Lyme disease.

Lyme IgM Results for Sofia 2 Lyme FIA with Sofia 2 Compared to Predicate Assay
IgM Method Comparison: 1st Tier PPA and NPA Analysis

		Predicate Lyme IgM				
		Positive	**Equivocal**	**Negative**	**% Agreement**	**95% CI**
Sofia 2 IgM	**Positive**	57	18	47	**PPA** = 82.4% (75/91)	73.2%-89.0%
	Negative	5	11	186	**NPA** =79.8% (186/233)	74.2%-84.5%
Total		62	29	233		

IgM Second Tier Testing
IgM Method Comparison: 2st Tier PPA Analysis

	Tier 1 + or ±	**IgM WB +**	**IgM WB -**
Predicate IgM	91	51	40
Sofia 2 IgM	122	52	70
Predicate + Sofia IgM	75	48	27

1st Tier PPA (95% CI)	82.4% (73.2-89.0%)	75/91
2nd Tier PPA (95% CI)	94.1% (83.5-98.6%)	48/51

Lyme IgG Results for Sofia 2 Lyme FIA with Sofia 2 Compared to Predicate Assay
IgG Method Comparison: 1st Tier PPA and NPA Analysis

		Predicate Lyme IgG			
		Positive	**Negative**	**% Agreement**	**95% CI**
Sofia 2 IgG	**Positive**	48	38	**PPA** = 88.9% (48/54)	77.5%-95.2%
	Negative	6	232	**NPA** = 85.9% (232/270)	81.2%-89.6%
Total		54	270		

IgG Second Tier Testing
IgG Method Comparison: 2st Tier PPA Analysis

	Tier 1 +	**IgG WB +**	**IgG WB -**
Predicate IgG	54	23	31
Sofia 2 IgG	86	23	63
Predicate + Sofia 2 IgG	48	22	26

1st Tier PPA (95% CI)	88.9% (77.5-95.2%)	48/54
2nd Tier PPA (95% CI)	95.7% (77.3->99.9)	22/23

5.12. Conclusion

These studies demonstrated the substantial equivalence of the Sofia 2 Lyme FIA to the Vidas Lyme IgG and Vidas Lyme IgM tests. Such studies are a critical element in establishing the fundamental safety and effectiveness of the product and its appropriateness for commercial distribution.