510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number: K173691

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Sofia Lyme FIA for use with Sofia 2 analyzers

C. Measurand:

IgM antibodies to *Borrelia burgdorferi* proteins

IgG antibodies to *Borrelia burgdorferi* proteins

D. Type of Test:

Fluorescent immunoassay (FIA), bi-directional lateral flow format

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Sofia Lyme FIA

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3830

2. Classification:

   Class II

3. Product code:

   LSR; Reagent, Borrelia Serological Reagent

4. Panel:

H. Intended Use:

1. Intended use(s):

   The Sofia Lyme FIA employs immunofluorescence for the rapid differential detection of human IgM and IgG antibodies to *Borrelia burgdorferi* from serum and plasma specimens from patients suspected of *B. burgdorferi* infection. This qualitative test is intended for use as an aid in the diagnosis of Lyme disease. A negative result does not preclude infection with *B. burgdorferi*. All positive results for IgM and/or IgG should be further tested by a corresponding second-tier 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 Sofia Lyme FIA may be used with Sofia or Sofia 2.

2. Indication(s) for use:

   Same as Intended Use(s)

3. Special conditions for use statement(s):

   Not Applicable (N/A)

4. Special instrument requirements:

   Sofia 2 Instrument

I. Device Description:

The Sofia 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, a patient serum or plasma specimen is obtained and added to a pre-filled vial containing the Lyme running buffer. The diluted sample is then pipetted into the round sample port in 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 10 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, and 10 minutes until both IgM and IgG positive results are received. This feature allows for earlier read times.

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

J. Substantial Equivalence Information:

1. Predicate device name(s):

Vidas Lyme IgM
Vidas Lyme IgG2.

Predicate 510(k) number(s):

K122979
K122986

3. Comparison with predicate:

Item	Proposed Device	Predicate IgM Device	Predicate IgG Device
Features	**Sofia Lyme FIA with Sofia 2**	**bioMerieux Vidas Lyme IgM**	**bioMerieux Vidas Lyme IgG**
Intended Use	The Sofia Lyme FIA employs immunofluorescence for the rapid differential detection of human IgM and IgG antibodies to *Borrelia burgdorferi* from serum and plasma specimens from patients suspected of *B. burgdorferi* infection. This qualitative test is intended for use as an aid in the diagnosis of Lyme disease. A negative result does not preclude infection with *B. burgdorferi*. All positive results for IgM and/or IgG should be further tested by a corresponding second-tier western blot assay. Test results are to be used in	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 Lyme FIA with Sofia 2**	**bioMerieux Vidas Lyme IgM**	**bioMerieux Vidas Lyme IgG**
	conjunction with information obtained from the patient's clinical evaluation and other diagnostic procedures. The Sofia Lyme FIA may be used with Sofia or Sofia 2.		
Instrument	Sofia 2 (and Sofia)	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	Sofia 2 - Potential for early read in Walk-Away Mode with Sofia 2. Sofia 2 will image cassette at 3, 5, 8, and 10 minutes until both IgM and IgG positive results are received. Sofia – 10 minutes	27 minutes	27 minutes
Specimen Types	Serum and plasma	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
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	One pre-filled vial containing	Sample diluent and wash	Sample diluent and wash

Item	Proposed Device	Predicate IgM Device	Predicate IgG Device
Features	**Sofia Lyme FIA with Sofia 2**	**bioMerieux Vidas Lyme IgM**	**bioMerieux Vidas Lyme IgG**
Buffer Solution	PBS	buffer	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.

K. Standard/Guidance Document Referenced (if applicable):

Establishing the Performance Characteristics of *In Vitro* Diagnostic Devices for the Detection of Antibodies to *Borrelia burgdorferi*

L. Test Principle:

Immunofluorescence

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

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. See Tables 1 and 2 for results.

Table 1. Sofia Lyme FIA with Sofia 2 Precision – Within Run

IgM or IgG Sample	IgM Positive		IgM % Positivity Total (n=96)	IgG Positive		IgG % Positivity Total (n=96)
	Run 1	Run 2		Run 1	Run 2	
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%

Table 2. Sofia Lyme FIA with Sofia 2 Precision – Between Operator

IgM or IgG Sample	% IgM Positivity		IgM % Positivity Total (n=96)	% IgG Positivity		IgG % Positivity Total (n=96)
	Operator1	Operator 2		Operator 1	Operator 2	
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%

The reproducibility of the Sofia Lyme FIA with Sofia 2 was evaluated at 3 different laboratories, 1 of which was Quidel. Two operators at each site tested a series of coded, contrived samples ranging from negative to moderate positive IgM and IgG concentrations. Testing occurred for a minimum of 5 separate days, spanning a period of approximately 2 weeks. See Table 3 for results.

Table 3. 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%)**

b. Linearity/assay reportable range: Not applicable (N/A)

c. Traceability, Stability, Expected values (controls, calibrators, or methods): N/A

d. Detection limit: N/A

e. Analytical specificity:

To determine the analytical specificity of the Sofia Lyme FIA with Sofia 2, 200 seemingly healthy individuals with no known history of physician-diagnosed Lyme disease were evaluated. Half of the samples (100) were collected from a non-endemic Lyme region while the other half of the samples (100) were collected from an

endemic Lyme region of the United States. Samples were tested on Sofia Lyme FIA and the predicate Lyme IgM and IgG assays. The Analytical Specificity results for Sofia Lyme FIA and the predicate devices are summarized in Table 4.

Table 4. Sofia Lyme FIA with Sofia 2 and Predicate Analytical Specificity

	n	Sofia IgM (% negative results)	Predicate IgM* (% negative results)	Sofia IgG (% negative results)	Predicate IgG (% negative results)
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.

f. Assay cut-off: N/A

i. Matrix Effects:

The purpose of this study is to compare plasma and serum using Sofia Lyme FIA with Sofia 2. Paired samples were used to compare matrix performance. The specimens tested were from non-selected prospectively collected donors, targeting 60 IgG positive and 60 IgM positive samples and selected (known positive) prospectively collected donors, targeting 60 IgG positive and 60 IgM positive samples.

Table 5. Sofia Lyme FIA with Sofia 2 – IgM Performance - Plasma vs. Serum

		Serum IgM		Total
		Positive	**Negative**	
Plasma IgM	**Positive**	129	3	132
	Negative	6	183	189
Total		135	186	321

Table 6. Sofia Lyme FIA with Sofia 2 – IgG Performance - Plasma vs. Serum

		Serum IgG		Total
		Positive	**Negative**	
Plasma IgG	**Positive**	86	12	98
	Negative	10	213	223
Total		96	225	321

2. Comparison studies:

a. Method comparison with predicate device:

A prospective study was performed using 325 serum samples collected from patients that were submitted for routine Lyme disease testing in the United States. These samples were prospectively collected from nine different clinical sites located in endemic areas of 6 states. Sofia Lyme FIA testing was performed at 3 laboratories,

including 1 Quidel site. The predicate Lyme IgM and IgG assays and western blot Lyme IgM and IgG assays were performed at a single laboratory site. First tier results for Sofia Lyme FIA using the Sofia 2 and the predicate assays are shown in Tables 7 and 8.

Table 7. First Tier Lyme IgM Results for Sofia Lyme FIA Tested on Sofia 2 Compared to Predicate Assay

		Predicate Lyme IgM				
		Positive	**Equivocal**	**Negative**	**% Agreement**	**95% CI**
Sofia IgM	Positive	57	18	46	PPA[2] = 84.3% (75/89)	75.2% - 90.5%
	Negative	5	9[1]	190	NPA = 80.5% (190/236)	75.0% - 85.1%
Total		62	27	236		

[1]Of the 9 specimens that were Sofia Lyme FIA negative and predicate equivocal, all 9 were negative by western blot

[2]Four specimens that were negative by the predicate were positive by Sofia Lyme FIA and confirmed positive by western blot

Table 8. First Tier Lyme IgG Results for Sofia Lyme FIA Tested on Sofia 2 Compared to Predicate Assay

		Predicate Lyme IgG			
		Positive	**Negative**	**% Agreement**	**95% CI**
Sofia IgG	Positive	47	27	PPA = 90.4% (47 / 52)	79.0% - 96.3%
	Negative	5	246	NPA = 90.1% (246/273)	86.0% - 93.2%
Total		52	273		

Second-Tier Testing

As recommended by CDC guidelines, second tier Western blot testing was performed on all positive (and equivocal with the predicate assay) samples when tested by either Sofia Lyme FIA or the predicate. The percent agreement between Sofia Lyme FIA and the predicate Lyme test are shown in Tables 9 and 10.

Table 9. IgM Second Tier Testing on Sofia 2

	Tier 1 + or ±	IgM WB +	IgM WB -
Predicate IgM	89	51	38
Sofia IgM	121	54	67
Predicate + Sofia IgM	75	50	25

1st Tier PPA (95% CI)	84.3% (75.2-90.5%)	75/89
2nd Tier PPA (95% CI)	98.0% (88.7-99.9%)	50/51

Table 10. IgG Second Tier Testing on Sofia 2

	Tier 1 +	IgG WB +	IgG WB -
Predicate IgG	52	21	31
Sofia IgG	74	22	52
Predicate + Sofia IgG	47	21	26

1st Tier PPA (95% CI)	90.4% (79.0-96.3%)	47/52
2nd Tier PPA (95% CI)	100% (81.8-100%)	21/21

b. Method comparison with original Sofia

The performance of Sofia Lyme FIA when used with Sofia vs. Sofia 2 was compared using a panel of plasma samples at one Quidel site. Panel members were prepared so that a broad range of negative and positive samples were evenly distributed across the dynamic range of the assay, including negative and high negative samples and low, moderate, and high positive samples. The Sofia vs. Sofia 2 comparison results for IgM and IgG are shown below in Tables 11 and 12 respectively.

Table 11. Sofia Lyme FIA – Sofia vs. Sofia 2 Comparison for IgM

TYPE IgM				
	Sofia			
	Pos	Neg		
Sofia 2 Pos	105	1[1]	PPA (95% CI)	105/111 = 94.6% (88.5% -97.7%)
Sofia 2 Neg	6[2]	123	NPA (95% CI)	123/124 = 99.2% (94.4% -97.9%)
Total	111	124		

[1] There was one discordant Sofia 2 positive/ Sofia negative result for IgM which was a high negative specimen.

[2] There were six discordant Sofia 2 negative/ Sofia positive results for IgM which were all low positive specimens.

Table 12. Sofia Lyme FIA – Sofia vs. Sofia 2 Comparison for IgG

TYPE IgG				
	Sofia			
	Pos	Neg		
Sofia 2 Pos	107	6[2]	PPA (95% CI)	107/110 = 97.3% (91.9% -99.4%)
Sofia 2 Neg	3[2]	119	NPA (95% CI)	119/125 = 95.2% (89.7% -98.0%)
Total	110	125		

[1] There were six discordant Sofia 2 positive/ Sofia negative results for IgG which were all high negative specimens.

[2] There were three discordant Sofia 2 negative/ Sofia positive results for IgG which were all low positive specimens.

3. Clinical Studies:

   a. Clinical Sensitivity: See K163713

   b. Clinical specificity: N/A

   c. Other clinical supportive data (when a. and b. are not applicable): N/A

N. Instrument Name:

Sofia 2

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes __X____ or No _____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes _X____ or No _____

P. Other Supportive Instrument Performance Characteristics Data Not Covered in The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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