**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**

**A. 510(k) Number:** K173496

**B. Purpose for Submission:** To obtain a substantial equivalence determination and FDA clearance for a new device

**C. Measurand:** Anti-*Borrelia burgdorferi* (IgM and/or IgG) antibodies

**D. Type of Test:** Enzyme Immunoassay

**E. Applicant:** Quidel Corporation

**F. Proprietary and Established Names:** Sofia 2 Lyme FIA and Sofia Lyme Control Set

**G. Regulatory Information:**

1. Regulation section: 21 CFR 866.3830; Treponema pallidum treponemal test reagents

2. Classification: Class II

3. Product code: LSR; Reagent, Borrelia Serological Reagent
   QCH; Serologic controls for microbiology assays

4. Panel: Microbiology

**H. Intended Use:**

1. Intended use(s):

**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.

2. Indication(s) for use: Same as Intended Use

3. Special conditions for use statement(s): N/A

4. Special instrument requirements: Sofia 2

**I. 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 for an automatically defined development time (Walk Away Mode) or pre-incubated on the bench top prior to loading into Sofia 2 (Read Now Mode). Sofia 2 scans the test strip, analyzes the fluorescent signal, and then displays two (2) test results: IgM and IgG.

**J. Substantial Equivalence Information:**

1. Predicate device name(s): Vidas Lyme IgM and Vidas Lyme IgG

2. Predicate 510(k) number(s): K122979 and K122986

3. Comparison with predicate:

Table 1: Similarities and Differences with the Predicate

| | Proposed Device | Predicate IgM Device | Predicate IgG Device |
|---|---|---|---|
| **Item** | **Sofia 2 Lyme FIA** | **Biomerieux Vidas Lyme IgM (K122979)** | **Biomerieux Vidas Lyme IgG (K122986)** |
| Intended Use | 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<br>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. | 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 burgdorferi* 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 burgdorferi* 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*. |
| 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 |

| | Proposed Device | Predicate IgM Device | Predicate IgG Device |
|---|---|---|---|
| **Item** | **Sofia 2 Lyme FIA** | **Biomerieux Vidas Lyme IgM (K122979)** | **Biomerieux Vidas Lyme IgG (K122986)** |
| 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 |
| 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 |

| | Proposed Device | Predicate IgM Device | Predicate IgG Device |
|---|---|---|---|
| **Item** | **Sofia 2 Lyme FIA** | **Biomerieux Vidas Lyme IgM (K122979)** | **Biomerieux Vidas Lyme IgG (K122986)** |
| 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.<br><br>•Built-in reference control line scanned by the analyzer to determine whether adequate flow occurred on the IgM side of the assay.<br><br>•Analyzer prevents used or expired cartridge from being read by the reader<br><br>•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):** N/A

**L. Test Principle:** Immunofluorescence

**M. Performance Characteristics (if/when applicable):**

*Note: Due to the inability to collect a finger-stick whole blood sample for certain studies, the performance characteristics are based on a combination of studies performed with either Sofia Lyme FIA or Sofia 2 Lyme FIA on either Sofia or Sofia 2 instruments which are equivalent. The sponsor has also established matrix equivalency between whole blood and serum/plasma to be able to use the data generated on Sofia instrument.*

1. Analytical performance:
   a. *Precision/Reproducibility:*

**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. The within run and between operator results are shown in the following two Tables.

Table 2: 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% |

Table 3: Sofia Lyme FIA with Sofia 2 Precision – Between Operator

| IgM or IgG Sample | % IgM Positivity | | IgM % Positivity | % IgG Positivity | | IgG % Positivity |
|---|---|---|---|---|---|---|
| | Operator1 | 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% |

**Reproducibility:** 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.

Table 4: 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:* N/A

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

*d. Detection limit:* N/A

*e. Analytical specificity:*

**Normal Population Study:** 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.

Table 5: Analytical Specificity Study

| | n | Sofia IgM (% negative) | Predicate IgM* (% negative) | Sofia IgG (% negative) | Predicate IgG (% negative) |
|---|---|---|---|---|---|
| **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

**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 with the Sofia Lyme FIA assay. Samples were characterized and obtained from commercial vendors and did not include any first or second tier Lyme testing results.

Table 6: Cross-Reactivity Study

| 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 (non-RMSF) | 3 | 0/3 | 0/3 |
| Rocky Mountain Spotted Fever (RMSF) | 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.

**Interferences:** A study was performed to assess potential interfering substances with the Sofia Lyme FIA with Sofia. The substances and concentrations tested are shown in the Table below. There was no interference or cross-reactivity results when tested with the Sofia Lyme FIA.

Table 7: 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 |

*f. Assay cut-off:*

The 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 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.

2. Comparison studies:

*a. Method comparison with predicate device:*

**Prospective Study:** A prospective study with Sofia 2 Lyme FIA with Sofia 2 was performed using matched blood specimens (finger-stick and serum/plasma) samples collected from 327 subjects suspected of and exhibiting symptoms of Lyme disease across 11 sites located in Lyme endemic regions throughout the United States. Sofia 2 Lyme FIA finger-stick whole blood testing was performed immediately at each of the 11 clinical sites by CLIA Waived operators. The predicate Lyme IgM and IgG assays and western blot Lyme IgM and IgG assays were performed at central reference laboratories that were different from the Sofia 2 testing sites. Out of 327 samples tested, three (3) invalid Sofia 2 test results were obtained, therefore 324 evaluable subjects were included in the analysis. First tier results for Sofia 2 Lyme FIA and the predicate assays are shown in the following two Tables.

Table 8: Percent Agreement with Predicate Device – IgM Results

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

Table 9: Percent Agreement with Predicate Device – IgG Results

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

**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 2 or the predicate. The percent agreement between Sofia 2 and the predicate Lyme test are shown in the following two Tables.

Table 10: 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 |

Table 11: 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 |

**CLIA Waiver Studies:** The studies are discussed in the CLIA Waiver Determination Decision Summary document (CW170015).

*b. Matrix comparison:*

The Sofia 2 Lyme FIA is to be used only with a finger-stick whole blood sample. 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. The results are summarized below and show performance is equivalent between the different sample types.

Table 12: 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%** |

3. Clinical studies:

*a. Clinical Sensitivity:*

**Clinical/Diagnostic Sensitivity Study:** To assess the sensitivity of the Sofia Lyme FIA with Sofia, 95 well-characterized clinically or culture confirmed Lyme disease serum samples were tested on Sofia Lyme and compared to the predicate IgM and IgG assays. The samples were blinded and tested on both Sofia Lyme FIA and the predicate Lyme IgM and Lyme IgG tests. The Sofia results are compared to those obtained with predicate Lyme IgM and IgG assays. Results for IgM and IgG are shown below.

Table 13: Case Confirmed Lyme Disease Samples – IgM Results

| | | **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.

Table 14: Case Confirmed Lyme Disease Samples – IgG Results

| | | **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% |

**CDC Panel Results:** A blinded serum panel consisting of 280 samples was obtained from the CDC and was evaluated internally using the Sofia Lyme FIA with Sofia. The Lyme disease samples are from physician-diagnosed patients with various stages of the disease. Early Lyme EM positive samples were collected days to weeks after disease onset. Late Lyme samples were collected months to years post disease onset. Samples from control individuals include sera from patients with lookalike or cross-reactive diseases/syndromes (syphilis, rheumatoid arthritis, fibromyalgia, mononucleosis, multiple sclerosis and severe periodontitis) and from healthy controls that are from individuals

residing in Lyme disease endemic and non-endemic regions who have no prior history of physician-diagnosed Lyme disease.

Table 15: Testing of CDC Lyme Disease 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% |

Table 16: Testing of CDC Lyme Disease 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% |

**Note:** The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC.

*b. Clinical specificity:* N/A

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

4. Clinical cut-off**:** N/A

5. Expected values/Reference range:

**Expected Values:** The rate of positivity observed in Lyme testing may vary depending on the time of year, the geographical location and disease prevalence for the season. Available patient demographics (age and gender), the number of samples tested and the number of samples that were positive for Sofia Lyme FIA and Sofia 2 Lyme FIA are summarized in the Table below.

Table 17: Expected Values

| **Study** | **Samples Tested** | | | **Age Range** | **Positive IgM/ Total Tested** | **Positive IgG/ Total Tested** |
|---|---|---|---|---|---|---|
| | **Total** | **Male** | **Female** | | | |
| **Prospective** | 324 | 165 | 159 | 4-84 | 122/324 | 86/324 |
| **Sensitivity** | 95 | 58 | 35 | 16-74 | 61/95 | 76/95 |
| **Endemic Negative** | 100 | 72 | 28 | 18-69 | 14/100 | 5/100 |
| **Non-Endemic Negative** | 100 | 68 | 32 | 20-64 | 7/100 | 2/100 |

## N. Proposed Labeling:

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

## O. Conclusion:

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