# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY ONLY

## I Background Information:

### A 510(k) Number

K203289

### B Applicant

Gold Standard Diagnostics

### C Proprietary and Established Names

Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| LSR | Class II | 21 CFR 866.3830 - Treponema Pallidum Treponemal Test Reagents | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

To obtain a substantial equivalence determination and FDA clearance for a new device and to obtain a substantial equivalence determination and FDA clearance for a modified intended use for several previously cleared medical devices. This regulatory filing follows the FDA guidance document titled “Bundling Multiple Devices or Multiple Indications in a Single Submission”1. For these devices, bundling is appropriate since the device review presented scientific and regulatory issues that were most efficiently addressed during a single review. In determining whether a bundled submission was appropriate FDA considered that: (i) the supporting data are similar; (ii) primarily one review division/group will be involved; and (iii) the devices or indications for use are similar.

### B Measurand:

Anti-*Borrelia burgdorferi* antibodies

## C Type of Test:

Enzyme-linked immunosorbent assay (ELISA)

## III Intended Use/Indications for Use:

### A Intended Use(s):

Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit

The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit is intended as a qualitative test for the detection of IgG and IgM class antibodies to VlsE and OspC antigens from *Borrelia burgdorferi* sensu stricto in human serum from symptomatic patients or people suspected of having Lyme disease. When used as the first-tier screening test, positive and equivocal results must be confirmed through additional testing by one of the following methods:

a) Standard two-tier test methodology (STTT) using an IgG and/or IgM blot testing following current interpretation guidelines, OR

b) Modified two-tier test methodology (MTTT) using one or more of the following three ELISA based assays: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test, Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test, Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test.

The assay can also be used as a second-tier confirmation test using the MTTT methodology when used with one or more of the following three ELISA based assays: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test, Gold Standard *Diagnostics Borrelia burgdorferi* IgG ELISA Test, Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test.

Positive test results by either the STTT or MTTT methodology are supportive evidence for the presence of antibodies and exposure to *Borrelia burgdorferi*, the cause of Lyme disease. A diagnosis of Lyme disease should be made based on the presence of *Borrelia burgdorferi* antibodies, history, symptoms, and other laboratory findings.

Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit

The Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit is intended as a qualitative test for the detection of IgG and IgM antibodies to *Borrelia burgdorferi* sensu stricto in human serum from symptomatic patients or people suspected of infection. When used as the first-tier screening test, positive and equivocal results must be confirmed through additional testing by one of the following methods:

a) Standard two-tier test methodology (STTT) using an IgG and or IgM blot testing following current interpretation guidelines, OR

b) Modified two-tier test methodology (MTTT) using the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test

The assay can also be used as a second-tier confirmation test using the MTTT methodology when used with when used with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test as the first-tier screening test.

Positive test results by either the STTT or MTTT methodology are supportive evidence for the presence of antibodies and exposure to *Borrelia burgdorferi*, the cause of Lyme disease. A diagnosis of Lyme disease should be made based on the presence of *Borrelia burgdorferi* antibodies, history, symptoms, and other laboratory findings.

Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test Kit

The Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test Kit is intended as a qualitative test for the detection of IgM antibodies to *B. burgdorferi* sensu stricto in human serum from symptomatic patients or people suspected of infection. When used as the first-tier screening test, positive and equivocal results must be supplemented through additional testing by one of the following methods:

a) Standard two-tier test methodology (STTT) using an IgM blot test following current interpretation guidelines, OR

b) Modified two-tier test methodology (MTTT) using the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test

The assay can also be used as a second-tier confirmation test using the MTTT methodology when used with when used with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test as the first tier screening test.

Positive test results by either the STTT or MTTT methodology are supportive evidence for the presence of antibodies and exposure to *Borrelia burgdorferi*, the cause of Lyme disease. A diagnosis of Lyme disease should be made based on the presence of *Borrelia burgdorferi* antibodies, history, symptoms, and other laboratory findings.

Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit

The Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit is intended as a qualitative test for the detection of IgG antibodies to *B. burgdorferi* sensu stricto in human serum from symptomatic patients or people suspected of infection. When used as the first-tier screening test, positive and equivocal results must be supplemented through additional testing by one of the following methods:

Standard two-tier test methodology (STTT) using an IgG blot test following current interpretation guidelines, OR

Modified two-tier test methodology (MTTT) using the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test.

The assay can also be used as a second-tier confirmation test using the MTTT methodology when used with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test as the first-tier screening test.

Positive test results by either the STTT or MTTT methodology are supportive evidence for the presence of antibodies and exposure to *Borrelia burgdorferi*, the cause of Lyme disease. A diagnosis of Lyme disease should be made based on the presence of *Borrelia burgdorferi* antibodies, history, symptoms, and other laboratory findings.

**B Indication(s) for Use:**
See Intended Use

**C Special Conditions for Use Statement(s):**
Rx - For Prescription Use Only

**D Special Instrument Requirements:**
N/A

## IV Device/System Characteristics:

**A Device Description:**
The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit is an Enzyme-linked immunosorbent assay (ELISA) for the qualitative detection of IgG and IgM antibodies to *Borrelia burgdorferi* in human serum.

During the test procedure, antibodies to *B. burgdorferi* (sensu stricto) if present in the human serum sample will bind to the antigens coated onto the wells forming antigen-antibody complexes. Excess antibodies are removed by washing. A conjugate of goat anti-human IgG/IgM antibodies conjugated with horseradish peroxidase is then added, which binds to the antigen-antibody complexes. Excess conjugate is removed by washing. This is followed by the addition of a chromogenic substrate, tetramethylbenzidine (TMB). If specific antibodies to the antigen are present in the patients' serum, a blue color will develop. The enzymatic reaction is then stopped with a stopping solution causing the contents of the well to turn yellow. The wells are read photometrically with a microplate reader at 450nm. OD values from controls or patient samples are converted to units by comparing to a cutoff value established using calibrators included with the kit. A result <9.0 units is negative and a result >11.0 units is positive. Samples with results of 9.0-11.0 units are considered equivocal.

The antigens used in the assay is a combination of recombinant VlsE and OspC from *B. burgdorferi* sensu stricto strain B31. The recombinants are produced in E. coli and purified by immobilized metal affinity chromatography (IMAC) via Polyhistidine-tag. The purity of each antigen is assayed by SDS-PAGE followed by Colloidal-Coomassie staining and western blotting.

The kit includes 12 x 8 well Antigen Coated strips, Conjugate, Substrate, Stop Solution, Wash Buffer, Diluent, Negative Control, Positive Control, and a Calibrator. The controls are provided to determine if the assay is functioning properly and to determine the antibody level. The reagents are sufficient for 96 determinations.

Calculation of Units and Results Interpretation

The OD of the blank value should be subtracted from all other OD values. The cutoff is determined by multiplying the Calibrator OD (or mean OD) by the Correction Factor value printed on the Calibrator vial label and on the Quality Control Certificate.

Cutoff = OD Calibrator x Correction Factor (C.F.)
Units* = (OD Controls or Samples / Cutoff) x 10

*Units are qualitative. They are values defined by the manufacturer.

The results are interpreted as follows:

| Units | Results | Interpretation |
|---|---|---|
| <9.0 | Negative | No detectable antibody. Result does not exclude *B. burgdorferi* infection |
| 9.0-11.0 | Equivocal | Initial evidence of antibodies to *B. burgdorferi* |
| >11.0 | Positive | Antibodies to *B. burgdorferi* presumptively detected |

## V Substantial Equivalence Information:

### A Predicate Device Name(s):
Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit

### B Predicate 510(k) Number(s):
K180264

### C Comparison with Predicate(s):

| Device & Predicate Device(s): | K203289 | K180264 |
|---|---|---|
| Device Trade Name | Device 1: Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit<br><br>Device 2: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit<br><br>Device 3: Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test Kit<br><br>Device 4: Gold Standard Diagnostics *Borrelia* | Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit |

| | | |
|---|---|---|
| | *burgdorferi* IgG ELISA Test Kit | |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | These are four ELISA assays for the qualitative detection of *B. Burgdorferi* antibodies in human serum. For a complete description of the Intended Use please see Item III B above. | The Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit is intended as a qualitative presumptive (first-step) test for the detection of IgG and IgM antibodies to *B. burgdorferi sensu stricto* in human serum from symptomatic patients or people suspected of infection. Positive and equivocal results must be supplemented by testing with a second-step Western blot assay. |
| Assay Format | Same | Antigen coated microtiter plate – 96 wells |
| Technology | Same | ELISA |
| Sample Matrix | Same | Serum |
| Sample Processing | Same | Dilute samples 1:100 in Diluent |
| Controls Provided | Same | Positive, Calibrator, Negative |
| Reagents Provided | Same | Diluent, Wash, Conjugate, Substrate, Stop Solution |
| Volumes | Same | 100 µL sample, 50 µL substrate, 50 µL stop solution |
| Incubation | Same | 15/15/15 minutes at room temperature |
| Reported Results | Same | Positive, Equivocal, Negative |
| Interpretation | Same | Optical density readings from Spectrophotometer |
| Results interpretation | Same | Convert to units.<br>Negative <9<br>Equivocal 9.0-11.0<br>Positive >11.0 |
| **General Device Characteristic Differences** | | |

| | | |
|---|---|---|
| Antigens | Recombinant VlsE and OspC from *B. burgdorferi* strain B31<br><br>*B. burgdorferi* B31 strain,<br>*B. burgdorferi* 2591 strain | *B. burgdorferi* B31 strain, *B. burgdorferi* 2591 strain, *B. burgdorferi recombinant* VlsE, B31 strain |

## VI Standards/Guidance Documents Referenced:

None.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

To determine the precision of the *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test, a within-lab precision study was conducted. A precision panel consisting of a negative sample, a high negative sample, a low positive sample, and a moderate positive sample, along with the kit controls, was tested in-house. The sample panel was masked and randomized. Each of the panel members was tested in duplicate, twice per day, for 12 days. The Within-Run, Between-Run, and Between-Days Standard Deviation and Coefficients of Variation (CV) were calculated. The results are summarized in the following table:

Table 1. Precision Study Results

| Sample | N | Mean Units | | Within-Run | Between-Run | Between-Day | Total |
|---|---|---|---|---|---|---|---|
| Moderate Positive | 48 | 35.8 | SD | 1.38 | 3.58 | 3.11 | 3.76 |
| | | | CV | 10.7% | 10.0% | 8.7% | 10.5% |
| Low Positive | 48 | 11.1 | SD | 0.44 | 0.85 | 0.73 | 0.95 |
| | | | CV | 8.6% | 7.7% | 6.6% | 8.5% |
| High Negative | 48 | 7.3 | SD | 0.32 | 0.59 | 0.48 | 0.66 |
| | | | CV | 9.2% | 8.1% | 6.6% | 9.0% |
| Negative | 48 | 1.6 | SD | 0.37 | 0.37 | 0.31 | 0.43 |
| | | | CV | 23.8% | 23.8% | 19.9% | 29.2% |
| Positive Control | 48 | 24.0 | SD | 0.62 | 1.35 | 1.18 | 1.45 |
| | | | CV | 6.2% | 5.6% | 4.9% | 6.1% |
| Calibrator | 48 | 11.1 | SD | 0.38 | 0.45 | 0.27 | 0.32 |
| | | | CV | 3.4% | 4.0% | 2.4% | 2.9% |
| Negative Control | 48 | 1.3 | SD | 0.22 | 0.28 | 0.22 | 0.35 |
| | | | CV | 27.7% | 21.5% | 17.0% | 26.6% |

Lot Variability

Lot variability was tested on three different production lots using a panel consisting of negative sample, a high negative sample, a low positive sample, and a moderate positive sample. The samples were tested with 24 replicates each. The within lot (intra-assay) and between lot (inter-assay) CV's were calculated. CV's ≤ 15% is considered acceptable performance. The results are summarized in the following table:

Table 2. Lot Variability Study Results

| Sample | | Moderate Positive | Low Positive | High Negative | Negative |
|---|---|---|---|---|---|
| Lot 1 Intra-assay | Mean Units | 22.4 | 12.1 | 6.8 | 1.1 |
| | SD | 0.764 | 0.417 | 0.457 | 0.052 |
| | CV | 3.4% | 3.4% | 5.3% | 9.1% |
| Lot 2 Intra-assay | Mean Units | 23.9 | 12.9 | 6.7 | 1.3 |
| | SD | 0.826 | 0.443 | 0.351 | 0.115 |
| | CV | 3.5% | 3.4% | 5.3% | 9.1% |
| Lot 3 Intra-assay | Mean Units | 22.8 | 11.1 | 6.0 | 1.0 |
| | SD | 0.709 | 0.405 | 0.286 | 0.083 |
| | CV | 3.1% | 3.6% | 4.8% | 8.0% |
| Inter-assay | Mean Units | 23.0 | 12.1 | 6.5 | 1.1 |
| | SD | 0.982 | 0.830 | 0.521 | 0.127 |
| | CV | 4.3% | 6.9% | 8.0% | 11.1% |

Reproducibility Study

A reproducibility panel consisting of a negative sample, a high negative sample, a low positive sample, and a moderate positive sample, along with the kit controls, was tested at three different sites. Each of the panel members was tested in triplicate, twice per day, for five days. The sample panel was masked and randomized. The Within-Run, Between-Run, Between-Days, and Between-Sites Standard Deviation and Coefficients of Variation (CV) were calculated. The results are summarized in the following table:

Table 3. Reproducibility Study Results

| Sample | N | Mean Units | | Within-Run | Between-Run | Between-Day | Between-Site | Total |
|---|---|---|---|---|---|---|---|---|
| Moderate Positive | 90 | 35.5 | SD | 3.19 | 2.65 | 1.37 | 3.11 | 3.14 |
| | | | CV | 9.0% | 7.5% | 3.9% | 8.8% | 8.9% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low Positive | 90 | 10.6 | SD | 0.95 | 0.65 | 0.21 | 0.88 | 0.94 |
| | | | CV | 9.0% | 6.2% | 2.0% | 8.4% | 8.9% |
| High Negative | 90 | 7.0 | SD | 0.92 | 0.85 | 0.41 | 0.81 | 0.90 |
| | | | CV | 13.1% | 12.1% | 5.9% | 11.6% | 12.9% |
| Negative | 90 | 1.5 | SD | 0.44 | 0.34 | 0.30 | 0.42 | 0.44 |
| | | | CV | 30.3% | 23.3% | 21.7% | 29.0% | 30.0% |
| Positive Control | 60 | 24.2 | SD | 1.39 | 1.26 | 0.51 | 1.32 | 1.37 |
| | | | CV | 5.7% | 5.2% | 2.1% | 5.5% | 5.7% |
| Calibrator | 90 | 11.1 | SD | 0.35 | 0.24 | 0.25 | 0.30 | 0.28 |
| | | | CV | 3.1% | 2.2% | 2.2% | 2.7% | 2.5% |
| Negative Control | 60 | 1.3 | SD | 0.32 | 0.28 | 0.16 | 0.32 | 0.31 |
| | | | CV | 25.2% | 22.2% | 12.8% | 25.7% | 24.8% |

2. Linearity:

Not Applicable.

3. Analytical Specificity/Interference:

**Analytical Specificity Study:** The analytical specificity was determined by testing 238 asymptomatic individuals' samples from endemic and non-endemic regions. The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test results are summarized in the following table:

Table 4. Analytical Specificity Study Results

| | **Number of Samples** | **Number Positive/Equivocal** | **Analytical Specificity** |
|---|---|---|---|
| **Endemic Region** | 132 | 4 | 97.0% |
| **Non-endemic Region** | 106 | 1 | 99.1% |

**Cross-reactivity Study:** A study using 226 samples was conducted to evaluate potential cross reactivity from different disease conditions. The samples were obtained from serum vendors who confirmed their positivity for each respective marker. The samples were tested on the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test. The results are summarized in the following table:

Table 5. Cross-reactivity Study Results

| **Organism/Disease State** | **Samples Tested (N)** | **Positive or Equivocal Result** |
|---|---|---|
| Tick borne Relapsing Fever | 4 | 3* |
| Treponemal Infections | 14 | 1 |
| Rickettsia | 8 | 0 |
| Ehrlichiosis IgG | 5 | 0 |

| | | |
|---|---|---|
| Ehrlichiosis IgM | 6 | 3* |
| Babesiosis | 16 | 6* |
| Leptospirosis | 10 | 2* |
| Parvovirus B19 | 12 | 0 |
| Influenza A&B | 17 | 0 |
| Epstein-Barr Virus | 11 | 0 |
| Cytomegalovirus | 14 | 0 |
| *H. pylori* | 12 | 0 |
| Fibromyalgia | 10 | 0 |
| Rheumatoid Arthritis | 10 | 0 |
| Herpes Simplex Virus 1&2 | 16 | 1* |
| Varicella Zoster virus | 14 | 1* |
| Autoimmune Disease | 47 | 3* |

* Samples were also positive by the predicate device

**Interfering Substances Study:** The effect of potential interfering substances on samples using the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test was evaluated. Five samples, two high negatives, two equivocals and a positive sample were spiked with high levels of interferants and were tested along with serum without spiked interferants. The recommended concentrations from the guideline "Interference Testing in Clinical Chemistry EP7-A3" from the Clinical and Laboratory Standards Institute were used. The tested substances did not affect the performance of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test.

Table 6. Interference Testing Results

| Substance | Concentration | Interference |
|---|---|---|
| Albumin | 60 mg/mL | None Detected |
| Bilirubin | 0.4 mg/mL | None Detected |
| Cholesterol | 4.0 mg/mL | None Detected |
| Hemoglobin | 10 mg/mL | None Detected |
| Triglycerides | 15 mg/mL | None Detected |

4. Assay Reportable Range:

Not Applicable.

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

Sample Stability Study

Fresh samples (a Positive, Low Positive, High Negative and Negative sample) were initially tested on the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test (day 0) then subsequently stored at 2 to 8°C for eight days. No significant changes in assay signal was observed. The data support a stability claim of seven days when stored at 2 to 8°C.

Freeze-thaw Study

A similar study was performed on samples stored frozen (including a positive, low positive, high negative, and negative sample). Samples were tested initially at day 0 and subsequently frozen at -20°C. The samples were then thawed, tested and frozen. This process was repeated for a total of four freeze-thaw cycles. No significant changes were observed over the course of the study supporting a freeze-thaw stability claim of three freeze-thaw cycles.

6. Detection Limit:

Not Applicable.

7. Assay Cut-Off:

The cutoff was determined by testing a total of 238 normal sera which consisted of 101 sera from an endemic region of Lyme disease and 95 sera from a non-endemic region of Lyme disease. The mean plus three standard deviations was used to determine the assay cutoff. A known positive sample was then diluted to produce a ready to use cutoff control. An additional 197 samples consisting of 125 samples from different phases of Lyme disease (79 samples from Dr. Steere and 46 samples from the CDC), and 72 negative Lyme disease samples (from CDC) but do have other diseases that may cause serologic cross-reactivity, were tested. A receiver operating characteristics (ROC) analysis was performed to evaluate the performance of the assay and confirm that the chosen cutoff provided the best compromise between sensitivity and specificity.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

**Method Comparison – STTT methodology**

**Prospective Study**: Comparison studies were conducted at three sites (one internal and two external reference laboratories) using prospective samples submitted for Lyme serology testing. Four hundred eighty-one (481) serum samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

Table 7. First-Tier Agreement

| | | **Predicate *B. burgdorferi* IgG/IgM ELISA** | | | |
|---|---|---|---|---|---|
| | | **Positive** | **Equivocal*** | **Negative** | **Total** |
| **Gold Standard Diagnostics *B. burgdorferi* VlsE-Ospc IgG/IgM ELISA Test Kit** | **Positive** | 39 | 6 | 6^ | 51 |
| | **Equivocal*** | 0 | 4 | 8^ | 12 |
| | **Negative** | 1** | 4** | 413 | 418 |
| | **Total** | 40 | 14 | 427 | 481 |

*Equivocal samples counted as positive
**Negative on IgG and IgM blot assays
^One sample positive on IgM blot assay

PPA: 90.7% (49/54) 95% CI: 79.7-96.9%
NPA: 96.7% (413/427) 95% CI: 94.6-98.2%

All positive and equivocal samples by the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and by the predicate IgG/IgM ELISA were tested by FDA cleared IgG and IgM blot assays. The results are summarized in the following tables:

Table 8. Second Tier Agreement – Standard Two-tiered Testing Algorithm

| Test System | Tier 1+ or Eqv. | Western Blot IgG/IgM + | Western Blot IgG/IgM - |
|---|---|---|---|
| **Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit** | 63 | 38 | 25 |
| **Predicate Assay** | 54 | 36 | 18 |
| **Predicate and Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit** | 49 | 36 | 13 |

The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test Kit identified a greater number of first-tier positive specimens, with slightly more western blot positive specimens captured.

Table 9. Second-tier Agreement – Standard Two-tiered Testing Algorithm

| | Predicate Assay - STTT | | |
|---|---|---|---|
| **Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA – STTT** | **Positive** | **Negative** | **Total** |
| **Positive** | 36 | 2 | 38 |
| **Negative** | 0 | 443 | 443 |
| **Total** | 36 | 445 | 481 |

Second-tier Positive Percent Agreement: 100% (36/36) 95% CI: 92.0-100%
Second-tier Negative Percent Agreement: 99.6% (443/445) 95% CI: 98.4-100%

**Method Comparison MTTT Algorithm – IgG/IgM**

Additional analyses were performed to determine the performance of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA test as a first-tier or second-tier assay in the modified two-tier testing (MTTT) methodology.

Four hundred eighty-one (481) serum samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. A total of 63 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA. A total of 54 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA. A total of 68 positive and equivocal samples were obtained with both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA and the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA.. In the STTT protocol the samples that were positive or equivocal (n=68) were tested with *B. burgdorferi* IgG and IgM blot tests. In the MTTT protocol the samples (n=68) were tested on a second ELISA, the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test. In the second-tier ELISA test, positive and equivocal results were considered positive. These two test methodologies are depicted in the figures below.

Figure 1. STTT-IgG/IgM Western Blot Algorithm (WB-STTT [IgG/IgM])

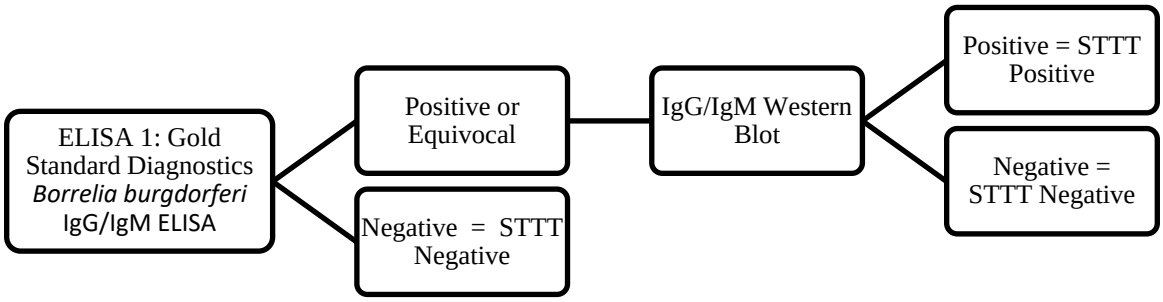
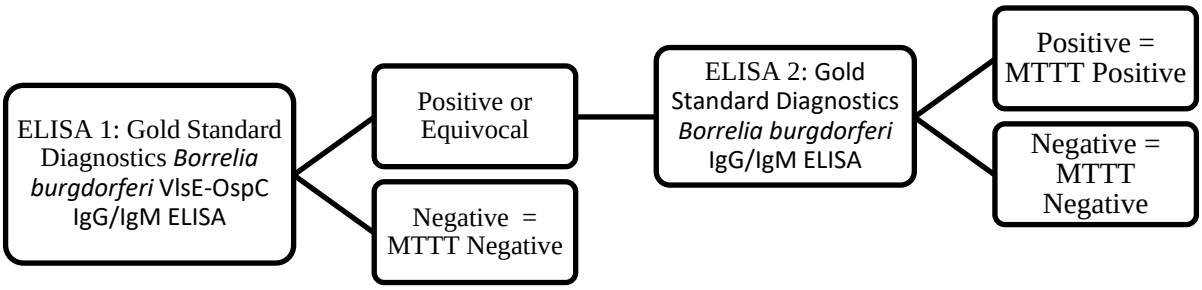



Figure 2. MTTT-IgG/IgM ELISA Algorithm (ELISA-MTTT [IgG/IgM])




Performance of the second-tier Gold Standard Diagnostics IgG/IgM ELISA was assessed by comparing results to second-tier western blot testing on only those samples positive by either first-tier test.

Table 10. Second-tier Performance Summary First-tier Positives Only - compared to WB

| | **Second-tier WB (IgG/IgM)** |
|---|---|

| | | Positive | Negative | Total |
|---|---|---|---|---|
| **Gold Standard Diagnostics IgG/IgM ELISA** | **Positive** | 36 | 18 | 54 |
| | **Negative** | 2 | 12 | 14 |
| **Total** | | 38 | 30 | 68 |

Positive Percent Agreement: 94.7% 95% CI: 82.3-99.4%
Negative Percent Agreement: 40.0% 95% CI: 22.7-59.4%

The results of the MTTT when compared to the STTT, including all samples that were part of the prospective study (n=481), are summarized in the following table:

Table 11. Performance Summary - ELISA-MTTT [IgG/IgM] compared to WB-STTT [IgG/IgM]

| | | WB-STTT (IgG/IGM) | | |
|---|---|---|---|---|
| | | **Positive** | **Negative** | **Total** |
| **Gold Standard Diagnostics ELISA-MTTT [IgG/IgM]** | **Positive** | 36 | 13 | 49 |
| | **Negative** | 0 | 432 | 432 |
| **Total** | | 36 | 445 | 481 |

Positive Percent Agreement: 100% (36/36) 95% CI: 90.3-100%
Negative Percent Agreement: 97.1% (432/445) 95% CI: 95.1-98.4%

The above performance table artificially inflates the negative percent agreement of the second-tier test since a large number of negatives are negative by both of the first-tier tests.

**Method Comparison – MTTT algorithm [IgG]**

The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test was utilized as the first-tier assay in a MTTT protocol. A total of 63 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorfer*i VlsE-OspC IgG/IgM ELISA. A total of 54 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA. A total of 68 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA and the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA. All positive and equivocal results were then tested on the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test as the second-tier testing. The results were compared to the standard two-tier testing (STTT) using the predicate B. burgdorferi IgG/IgM ELISA followed by testing all positive and equivocal results on the predicate *B. burgdorferi* IgG blot test.These test methodologies are summarized in Figure 3 and Figure 4 below.

Figure 3. STTT-IgG Western Blot Algorithm (WB-STTT [IgG])

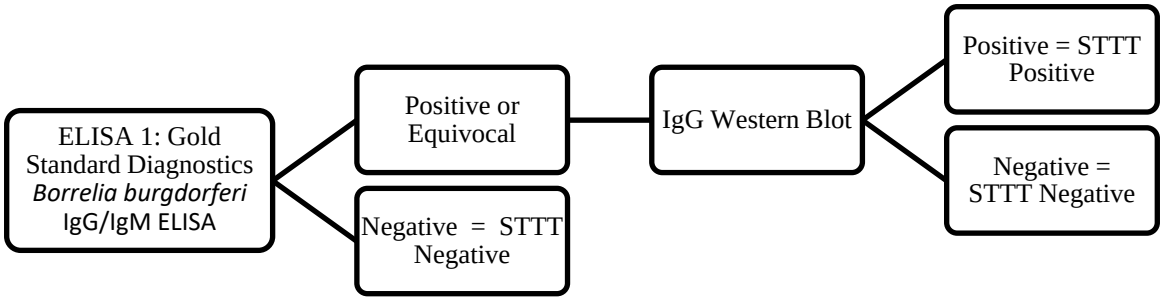
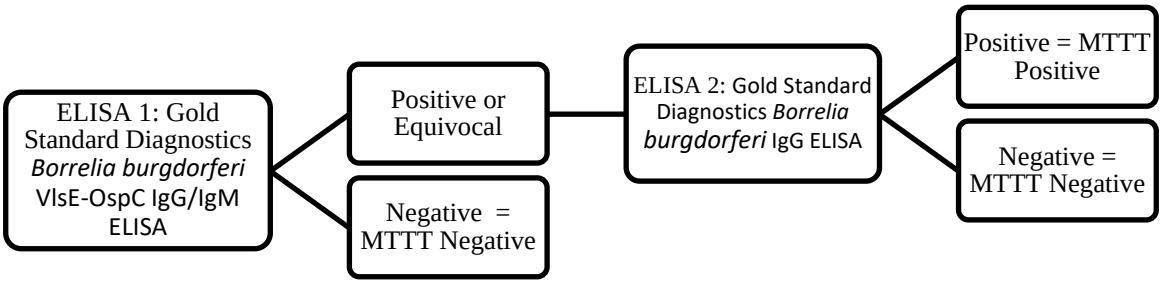



Figure 4. MTTT-IgG ELISA Algorithm (ELISA-MTTT [IgG])




Performance of the second-tier Gold Standard Diagnostics IgG ELISA was assessed by comparing results to second-tier western blot testing on only those samples positive by either first-tier test.

Table 12. Second-tier Performance Summary First-tier Positives Only - compared to WB

| | | **Second-tier WB [IgG]** | | |
|---|---|---|---|---|
| | | **Positive** | **Negative** | **Total** |
| **Gold Standard Diagnostics IgG ELISA** | **Positive** | 23 | 15 | 38 |
| | **Negative** | 0 | 30 | 30 |
| **Total** | | 23 | 45 | 68 |

Positive Percent Agreement: 100.0% (23/23) 95% CI: 85.2-100%
Negative Percent Agreement: 66.7% (30/45) 95% CI: 51.1-80.0%

The results of the MTTT when compared to the STTT, including all samples that were part of the prospective study (n=481), are summarized in the following table:

Table 13. Performance Summary - ELISA-MTTT [IgG] compared to WB-STTT [IgG]

| | **WB-STTT [IgG]** | | |
|---|---|---|---|
| | **Positive** | **Negative** | **Total** |

| | | | | |
|---|---|---|---|---|
| **Gold Standard Diagnostics ELISA-MTTT [IgG]** | **Positive** | 23 | 15 | 38 |
| | **Negative** | 0 | 443 | 443 |
| **Total** | | 23 | 458 | 481 |

Positive Percent Agreement: 100% (23/23) 95% CI: 85.2-100%
Negative Percent Agreement: 96.7% (443/458) 95% CI: 94.7-98.2%

The above performance table artificially inflates the negative percent agreement of the second-tier test since a large number of negatives are negative by the first tier tests.

**Method Comparison – MTTT Methodology (IgM)**

The Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test was utilized as the first-tier assay in a MTTT protocol. All positive and equivocal results were then tested on the Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test as the second-tier testing. The results were compared to the standard two-tier testing (STTT) using the predicate *B. burgdorferi* IgG/IgM ELISA followed by testing all positive and equivocal results on the predicate *B. burgdorferi* IgM blot test.

Comparison studies were conducted at three sites (one internal and two external reference laboratories) using prospective samples submitted for Lyme serology testing. Four hundred eighty-one (481) serum samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. A total of 63 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA. A total of 54 positive and equivocal samples were obtained with the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA. A total of 68 positive and equivocal samples were obtained with both assays. In the STTT protocol the samples that were positive or equivocal (n=68) were tested with a *B. burgdorferi* IgM blot test. In the MTTT protocol the samples (n=68) were tested on a second ELISA, the Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA Test. In the second-tier ELISA test, positive and equivocal results were considered positive. These test methodologies are summarized in Figure 5 and Figure 6 below.

Figure 5. STTT-IgM Western Blot Algorithm (WB-STTT [IgM])

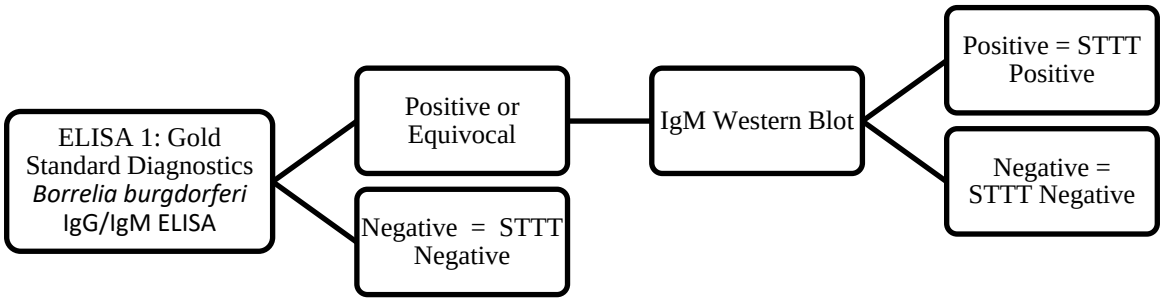
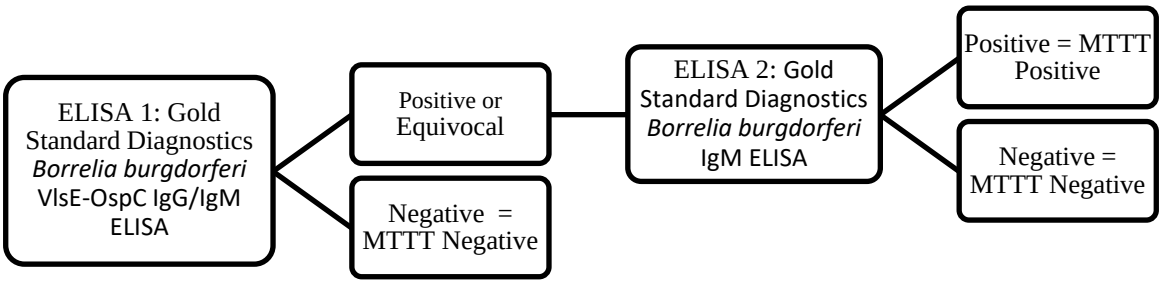



Figure 6. MTTT-IgM ELISA Algorithm (ELISA-MTTT [IgM])




Performance of the second-tier Gold Standard Diagnostics IgM ELISA was assessed by comparing results to second-tier western blot on only those samples positive by the either first-tier test.

Table 14. Second-tier Performance Summary First-tier Positives Only - compared to WB

| | | **Second-tier WB [IgM]** | | |
|---|---|---|---|---|
| | | **Positive** | **Negative** | **Total** |
| **Gold Standard Diagnostics IgM ELISA** | **Positive** | 20 | 22 | 42 |
| | **Negative** | 1 | 25 | 26 |
| **Total** | | 21 | 47 | 68 |

Positive Percent Agreement: 95.2% (20/21) 95% CI: 76.2-99.9%
Negative Percent Agreement: 53.2% (25/47) 95% CI: 38.1-67.9%

The results of the MTTT when compared to the STTT, including all samples that were part of the prospective study (n=481), are summarized in the following table:

Table 15. Performance Summary - ELISA-MTTT [IgM] compared to WB-STTT [IgM]

| | | **WB-STTT (IgM)** | | |
|---|---|---|---|---|
| | | **Positive** | **Negative** | **Total** |
| **Gold Standard Diagnostics-MTTT (IgM)** | **Positive** | 18 | 22 | 40 |
| | **Negative** | 1 | 440 | 441 |
| **Total** | | 19 | 462 | 481 |

Positive Percent Agreement: 94.7% (18/19) 95% CI: 74.0-99.9%
Negative Percent Agreement: 95.2% (440/460) 95% CI: 92.9-97.0%

The above performance table artificially inflates the negative percent agreement of the second-tier test since a large number of negatives are negative by the first tier tests.

2. Matrix Comparison:

Not Applicable.

## C Clinical Studies:

1. Clinical Sensitivity:

**STTT methodology**

**Sensitivity Study:** A sensitivity study was performed on 125 clinically characterized samples. The samples encompass early, disseminated, and late stages of Lyme disease. The samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

Table 16. Sensitivity Study Results – STTT Methodology

| | N | Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA | | Predicate *B. burgdorferi* IgG/IgM ELISA | |
|---|---|---|---|---|---|
| **Disease Stage** | | **Positive/Eqv.** | **% Agreement with Clinical Diagnosis** | **Positive/Eqv.** | **% Agreement with Clinical Diagnosis** |
| **Early** | 62 | 39 | 62.9% | 41 | 66.1% |
| **Disseminated** | 22 | 22 | 100% | 20 | 90.9% |
| **Late** | 41 | 40 | 97.6% | 41 | 100% |

**CDC Reference Panel:** A panel of 280 positive and negative specimens from the Centers of Disease Control (CDC) for Lyme disease detection was tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test and on the predicate device. The results are presented as a means to convey further information on the performance of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test with a masked characterized serum panel. This does not imply an endorsement of the assay by the CDC. The results are summarized in the following table:

Table 17. CDC Reference Panel Testing Results – STTT Methodology

| Sample Category | Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test | | | | Predicate *B. Burgdorferi* IgG/IgM ELISA | | | |
|---|---|---|---|---|---|---|---|---|
| | **Pos. or Eqv.** | **Neg.** | **PPA/ NPA** | **95% CI** | **Pos. or Eqv.** | **Neg.** | **PPA/ NPA** | **95% CI** |
| **Early Lyme (N = 60)** | 49 | 11 | 81.7% | 69.6-90.5% | 46 | 14 | 76.7% | 64.0-86.6% |
| **Cardiac Lyme (N = 3)** | 2 | 1 | 66.7% | 9.4-99.2% | 3 | 0 | 100% | 29.2-100% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Neurological Lyme (N = 7)** | 7 | 0 | 100% | 59.0-100% | 6 | 1 | 85.7 | 42.1-99.6% |
| **Late Lyme (N = 20)** | 20 | 0 | 100% | 83.2-100% | 20 | 0 | 100% | 83.2-100% |
| **Healthy Controls (N = 100)** | 3 | 97 | 97% | 91.5-99.4% | 0 | 100 | 100% | 96.4-100% |
| **Disease Controls (N = 90)** | 4 | 86 | 95.6% | 89.0-98.8% | 16 | 74 | 82.2% | 72.7-89.5% |

Cumulatively, these data establish equivalence of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA to the predicate device when utilized as a first-tier test for Lyme disease.

**MTTT Methodology [IgG/IgM]**

**Sensitivity Study:** A sensitivity study was performed on 125 clinically characterized samples. The samples encompassed early, disseminated, and late stages of Lyme disease. The samples were tested using both the Gold Standard Diagnostics MTTT algorithm and the predicate STTT algorithm. The results are summarized in the following table:

Table 18. Sensitivity Study Results – Comparison of ELISA-MTTT [IgG/IgM] and WB-STTT [IgG/IgM] algorithms

| **Disease Stage** | **N** | **Gold Standard Diagnostics ELISA-MTTT [IgG/IgM]** | | **WB-STTT [IgG/IgM]** | |
|---|---|---|---|---|---|
| | | **Pos. or Eqv.** | **% Agreement with Clinical Diagnosis** | **Pos. or Eqv.** | **% Agreement with Clinical Diagnosis** |
| Early | 62 | 38 | 61.3% | 39 | 62.9% |
| Disseminated | 22 | 20 | 90.9% | 20 | 90.9% |
| Late | 41 | 40 | 97.6% | 40 | 97.6% |

**CDC Reference Panel:** A panel of 280 positive and negative specimens from the Centers of Disease Control (CDC) for Lyme disease detection was tested using both the Gold Standard Diagnostics MTTT algorithm and on the predicate STTT algorithm. The results are summarized in the following table:

Table 19. CDC Reference Panel Test Results – Comparison of ELISA-MTTT [IgG/IgM] and WB-STTT [IgG/IgM] algorithms

| **Sample Category** | **Gold Standard Diagnostics ELISA-MTTT [IgG/IgM]** | | | | **WB-STTT [IgG/IgM]** | | | |
|---|---|---|---|---|---|---|---|---|
| | **Pos. or Eqv.** | **Neg.** | **PPA/ NPA** | **95% CI** | **Pos. or Eqv.** | **Neg.** | **PPA/ NPA** | **95% CI** |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Early Lyme (N = 60)** | 46 | 14 | 76.7% | 64.0-86.6% | 37 | 22 | 61.7% | 48.2-74.0% |
| **Cardiac Lyme (N = 3)** | 2 | 1 | 66.7% | 9.4-99.2% | 2 | 1 | 66.7% | 9.4-99.2% |
| **Neurological Lyme (N = 7)** | 6 | 1 | 85.7% | 42.1-99.6% | 6 | 1 | 85.7% | 42.1-99.6% |
| **Late Lyme (N = 20)** | 20 | 0 | 100% | 83.2-100% | 20 | 0 | 100% | 83.2-100% |
| **Healthy Controls (N = 100)** | 0 | 100 | 100% | 96.4-100% | 0 | 100 | 100% | 96.4-100% |
| **Disease Controls (N = 90)** | 1 | 89 | 98.9% | 94.0-100% | 4 | 86 | 95.6% | 89.0-98.8% |

Cumulatively, these data establish equivalence of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA to the predicate device when utilized as a first-tier test as part of an MTTT algorithm using the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA.

**MTTT Methodology [IgG]**

**Sensitivity Study:** A sensitivity study was performed on 125 clinically characterized samples. The samples encompass early, disseminated, and late stages of Lyme disease. The samples were tested on both the Gold Standard Diagnostics ELISA-MTTT [IgG] algorithm and on the predicate WB-STTT [IgG] algorithm. The results are summarized in the following table.

Table 20. Sensitivity Study Results - Comparison of ELISA-MTTT [IgG] and WB-STTT [IgG] algorithms

| **Disease Stage** | **N** | **Gold Standard Diagnostics ELISA-MTTT [IgG]** | | **WB-STTT [IgG]** | |
|---|---|---|---|---|---|
| | | **Pos. or Eqv.** | **% Agreement with Clinical Diagnosis** | **Pos. or Eqv.** | **% Agreement with Clinical Diagnosis** |
| Early | 62 | 30 | 48.4% | 5 | 8.1% |
| Disseminated | 22 | 18 | 81.8% | 6 | 27.3% |
| Late | 41 | 40 | 97.6% | 39 | 95.1% |

**CDC Reference Panel:** A panel of 280 positive and negative specimens from the Centers of Disease Control (CDC) for Lyme disease detection was tested using both the Gold Standard Diagnostics ELISA-MTTT [IgG] algorithm and the predicate WB-STTT [IgG] algorithm. The results are summarized in the following table:

Table 21. CDC Reference Panel Test Results - Comparison of ELISA-MTTT [IgG] and WB-STTT [IgG] algorithms

| Sample Category | Gold Standard Diagnostics ELISA-MTTT [IgG] | | | | Predicate WB-STTT [IgG] | | | |
|---|---|---|---|---|---|---|---|---|
| | Pos. | Neg. | PPA/ NPA | 95% CI | Pos. | Neg. | PPA/ NPA | 95% CI |
| **Early Lyme (N = 60)** | 36 | 24 | 60.0% | 46.5-72.4% | 15 | 22 | 25.0% | 14.7-37.9% |
| **Cardiac Lyme (N = 3)** | 2 | 1 | 66.7% | 9.4-99.2% | 1 | 2 | 33.3% | 0.8-90.6% |
| **Neurological Lyme (N = 7)** | 6 | 1 | 85.7% | 42.1-99.6% | 1 | 6 | 14.3% | 0.3-57.9% |
| **Late Lyme (N = 20)** | 20 | 0 | 100% | 83.2-100% | 20 | 0 | 100% | 83.2-100% |
| **Healthy Controls (N = 100)** | 0 | 100 | 100% | 96.4-100% | 0 | 100 | 100% | 96.4-100% |
| **Disease Controls (N = 90)** | 0 | 90 | 100% | 96.0-100% | 0 | 90 | 100% | 96.0-100% |

Cumulatively, these data establish equivalence of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA to the predicate device when utilized as a first-tier test as part of an MTTT algorithm using the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA.

**MTTT Methodology [IgM]**

**Sensitivity Study:** A sensitivity study was performed on 125 clinically characterized samples. The samples encompass early, disseminated, and late stages of Lyme disease. The samples were tested using both the Gold Standard Diagnostics ELISA-MTTT [IgM] algorithm and the predicate STTT-IgM algorithm. The results are summarized in the following table:

Table 22. Sensitivity Study Results - Comparison of ELISA-MTTT [IgM] and WB-STTT [IgM] algorithms

| Disease Stage | N | Gold Standard Diagnostics ELISA-MTTT [IgM] | | Predicate WB-STTT [IgM] | |
|---|---|---|---|---|---|
| | | Pos. or Eqv. | % Agreement with Clinical Diagnosis | Pos. or Eqv. | % Agreement with Clinical Diagnosis |
| Early | 62 | 39 | 62.9% | 36 | 58.1% |

| | | | | | |
|---|---|---|---|---|---|
| Disseminated | 22 | 22 | 100% | 20 | 90.9% |
| Late | 41 | 34 | 82.9% | 10 | 24.4% |

**CDC Reference Panel:** A panel of 280 positive and negative specimens from the Centers of Disease Control (CDC) for Lyme disease detection was tested on both the Gold Standard Diagnostics MTTT- IgG and on the predicate STTT- IgG. The results are summarized in the following table:

Table 23. CDC Reference Panel Test Results – Comparison of ELISA-MTTT [IgM] and WB-STTT [IgM] algorithms

| Sample Category | Gold Standard Diagnostics ELISA-MTTT [IgM] | | | | Predicate WB-STTT [IgM] | | | |
|---|---|---|---|---|---|---|---|---|
| | Pos. | Neg. | PPA/ NPA | 95% CI | Pos. | Neg. | PPA/ NPA | 95% CI |
| **Early Lyme (N = 60)** | 46 | 14 | 76.7% | 64.0-86.6% | 30 | 30 | 50% | 36.8-63.2% |
| **Cardiac Lyme (N = 3)** | 2 | 1 | 66.7% | 9.4-99.2% | 2 | 1 | 66.7% | 9.4-99.2% |
| **Neurological Lyme (N = 7)** | 7 | 0 | 100% | 59.0-100% | 6 | 1 | 85.7% | 42.1-99.6% |
| **Late Lyme (N = 20)** | 16 | 4 | 80% | 56.3-94.3% | 9 | 11 | 45.0% | 23.1-68.5% |
| **Healthy Controls (N = 100)** | 0 | 100 | 100% | 96.4-100% | 0 | 100 | 100% | 96.4-100% |
| **Disease Controls (N = 90)** | 3 | 87 | 96.7% | 90.6-99.3 | 1 | 89 | 98.9% | 94.0-100% |

Cumulatively, these data establish equivalence of the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA to the predicate device when utilized as a first-tier test as part of an MTTT algorithm using the Gold Standard Diagnostics *Borrelia burgdorferi* IgM ELISA.

2. Clinical Specificity:

   Not Applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not Applicable.

**D Clinical Cut-Off:**

Not Applicable.

## E Expected Values/Reference Range:

The range of values and positivity rate among different studies and population for the Gold Standard Diagnostics *Borrelia burgdorferi* VlsE-OspC IgG/IgM ELISA Test are as follows:

| Population | # Samples | Unit Results | | | Qualitative Results | |
|---|---|---|---|---|---|---|
| | | Mean | Range | Std. Dev. | # Positive /Equivocal | % Positive /Equivocal |
| Normal Endemic | 132 | 2.8 | 0.3 – 20.3 | 2.8 | 4 | 3.0% |
| Normal Non-Endemic | 106 | 2.4 | 0.3 – 9.0 | 1.4 | 1 | 0.9% |
| Prospective Study | 481 | 5.4 | 0.7 – 45.7 | 6.4 | 63 | 13.1% |
| Sensitivity Study | 125 | 21.3 | 1.3 – 37.2 | 10.5 | 100 | 80.0% |

## 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.