

K971170

Section 12 510(k) SUMMARY

Submitted By:

FEB 17 1998

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Contact Person:

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Date of Preparation:

19 March 1997 Revised on 4 February 1998

Product Name and Information

1. Name and Address of Owner/Operator, and Manufacturer

Owner/Operator:

Cambridge Biotech Corporation
A Wholly Owned Subsidiary of bioMérieux Vitek, Inc.
1500 East Gude Drive
Rockville, MD 20850-5307

Manufacturer:

Cambridge Biotech Corporation
A Wholly Owned Subsidiary of bioMérieux Vitek, Inc.
1500 East Gude Drive
Rockville, MD 20850-5307

2. Product Name

Trade Name: Cambridge Biotech *Borrelia burgdorferi*
Human Lyme IgM Western Blot kit

Common Name: Lyme IgM Western Blot kit

Classification Name: Reagent, Borrelia Serological Reagent

3. Claim of Substantial Equivalence

The characterized samples used for the establishment of Substantial Equivalence have a clinical diagnosis of Lyme Disease based on the probability of exposure/infection (tick bite and/or patient presence in potential tick habitats in an endemic region within 30 days prior to the onset of EM (erythema migrans)), *Borrelia* isolation by culture (where possible), or, for non-EM patients, the presentation of Late Lyme clinical manifestations (e.g., cardiac, joint-involvement, or neurological symptoms).

Each of the clinical trial sites provided specimens that were well-characterized by the site using Lyme-specific serological analyses, including EIA and Western Blot testing.

Substantial equivalence of this device is based on the assessment of performance of the device in these clinical trials in which the well-characterized, archived Lyme Disease specimens, the Centers for Disease Control Lyme Disease Serum Panel, normal donor specimens (from endemic and non-endemic regions), and samples from diverse disease conditions were analyzed.

4. Description

The device is a Western Blot assay. Proteins and other antigenic components of the *Borrelia* spirochete are fractionated by Polyacrylamide Gel Electrophoresis in the presence of Sodium Dodecylsulfate. The separated proteins are electrophoretically transferred from the gel to nitrocellulose membranes, which are subsequently blocked to minimize non-specific binding and cut into strips. These nitrocellulose strips with *Borrelia burgdorferi* antigens are then reacted with diluted serum and controls (positive and negative sera of defined reactivity) during an incubation period.

During the incubation period, human antibodies specific to the *B. burgdorferi* antigens, if present in the sample or control, will bind to the antigen to which they have affinity. Unbound serum and non-specific antibodies are washed from the strip. Detection of bound IgM antibodies is accomplished by reacting and incubating the strips with a solution containing anti-human IgM antibodies conjugated with alkaline phosphatase. Unbound conjugate antibodies are removed by washing. The qualitative assessment of the detected IgM antibodies is then accomplished by the reaction of the alkaline phosphatase with a chemical substrate, which is cleaved into a colored, insoluble product that can be visualized. The determination of the reactivity of each unknown specimen is accomplished by comparison of the identified, visualized bands to the Band Identifying and Band Intensity Controls.

5. Intended Use

The Cambridge Biotech *Human Lyme B. burgdorferi* IgM Western Blot is an *in vitro* test system for the qualitative detection of human Immunoglobulin M (IgM) antibodies to *Borrelia burgdorferi* antigens in human serum. The Cambridge Biotech *Human Lyme B. burgdorferi* IgM Western Blot is intended for use in testing human serum samples which have demonstrated positive or equivocal responses using EIA or IFA test procedures to provide supportive evidence of infection with *Borrelia burgdorferi*.

The Cambridge Biotech *Human Lyme B. burgdorferi* IgM Western Blot can be used during the acute phase (0-4 weeks of symptoms onset) of *B. burgdorferi* infection. After this period, infected patients are usually found to be Western Blot positive for IgG. A positive IgM test alone is not recommended for use in determining active disease in persons with illness of longer than one month.

6. Performance Summary

The report of the complete clinical trial for the Cambridge Biotech Human Lyme IgM kit is contained in this section. Data for IgG and IgM have not been interpreted together, but separately, as will be required in clinical settings.

From a summary of the clinical trial data, the following performance characteristics are described:

Specificity

Specificity of the device was determined from analysis of testing results of normal donor (from endemic and non-endemic regions) and disease specimens (1062 total samples) and was shown to be 97.5%, with 95% confidence intervals of 96.6% to 98.5%.

Sensitivity

Sensitivity of the device was determined from analysis of test results of characterized Lyme disease specimens (296 total samples) that were drawn at different times after onset of disease:

**Sensitivity of the Cambridge Biotech Human Lyme *B. burgdorferi* IgM Western Blot
Relative to Lyme Disease Clinical Diagnosis and Treatment
including Results by Draw Time**

Disease Presentation	Draw Time (months)	Total Number of Specimens	Number By Draw Time	Number of Specimens Positive	Specimens Positive By Draw Time	Sensitivity	95% CL
Before Treatment	<1	102	100	58	56	57%	47.3-66.5%
	1-2		2		2		
	2-12		0		0		
After Treatment	<1	131	40	84	27	64%	55.9-72.3%
	1-2		51		35		
	2-12		40		22		
Lyme Late	<1	64	0	25	0	39%	27.1-51.0%
	1-2		0		0		
	2-12		64		25		

The Draw Time is the time from disease onset to specimen collection. The specimens were taken from 169 individual patients. Second draws were done on 92 of the 169 patients, third draws were done on 36 of those patients. The specimens from patients under antibiotic treatment may interfere with positive results.

Precision

Six IgM Controls were tested in duplicate on each of three days at three test sites, totaling 18 replicates per control for all sites. All three sites were in 100% agreement for the disposition of the six IgM Controls. Additionally, all three sites were in 100% agreement for the three diagnostic bands (p41, p39, and p23) for all six controls on every day of testing.

Reproducibility

Ten positive and negative specimens from the CDC 47-member panel were tested at four sites. There was 100% agreement for the IgM disposition scores with the 20 specimens at all four sites. Eighty six point seven percent (86.7%) of the three diagnostic bands of all 20 specimens were scored identically at all four test sites. In addition, a 94% overall agreement was shown between the scoring of positive IgM bands by the sites and the expected IgM band score results.

Agreement with Expected Results Across Four Sites

Site	Number of Correct Bands	Percentage of Correct Bands	Correct Number of Interpretations	Percent (%)
Site 1	25/27	93%	20/20	100
Site 2	25/27	93%	20/20	100
Site 3	26/27	96%	20/20	100
Site 4	25/27	93%	20/20	100
Total	101/108	94%	80/80	100

7. Determination of Threshold Intensity

The threshold determination was originally performed by analysis of IgM sensitivity and specificity panels. The intensity of weakly reactive Lyme antibody-positive samples (n = 3) were compared to the intensities of highly reactive Lyme antibody-negative samples (n = 10) in preclinical testing to demonstrate that the threshold appropriately differentiated positive and negative specimens. The negative specimens included both normal donors and samples from patients with potentially cross-reactive conditions or infections. The p41 band was chosen as the intensity indicator for all bands except p23. The p23 band is used to score p23 bands, due to its diffuse nature. Subsequent lots of the Control have been approved based on continued demonstration of this characteristic.

8. Conclusions

Based on the clinical performance, this device has been shown to be safe and effective for the intended use in the qualitative detection of human Immunoglobulin M (IgM) antibodies in serum or plasma to *Borrelia burgdorferi* antigens, and as a supplemental, more specific, test to aid in the diagnosis of infection or exposure to *Borrelia burgdorferi*, the causative agent of Lyme disease.



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. Wole Edwin
Director of Quality Assurance
and Regulatory Affairs
Cambridge Biotech
1500 East Gude Drive
Rockville, MD 20850-5307

FEB 17 1998

Re: K971170
Trade Name: Cambridge Biotech Human Lyme Borrelia burgdorferi
IgM Western Blot Kit
Regulatory Class: II
Product Code: LSR
Dated: December 3, 1997
Received: December 3, 1997

Dear Mr. Edwin:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

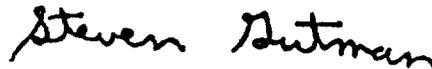
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

