SEP 2 1 1999

K991062

510(k) Safety and Effectiveness Summary

Submitted by:

Immunetics, Inc.
63 Rogers Street
Cambridge, MA 02142

Contact Person:

Andrew E. Levin, Ph.D.
Scientific Director

(617) 492 - 5416

Date of Preparation:

September 9, 1999

1. Name and Address of Owner/Operator and Manufacturer

Immunetics, Inc.
63 Rogers Street
Cambridge, MA 02142

2. Product Name

Trade Name: QualiCode™ *B. burgdorferi* IgM Western Blot Kit

Common Name: *B. burgdorferi* IgM Western Blot Kit

3. Claim of Substantial Equivalence

The characterized samples used for the establishment of Substantial Equivalence were obtained from patients with a clinical diagnosis of Lyme Disease in accordance with the CDC case definition, i.e. based on the presence of EM (erythema migrans) or the presentation of late Lyme clinical manifestations (e.g., arthritic, cardiac, or neurological symptoms). Infection was confirmed by culture of *Borrelia* from biopsies in many examples.

Each of the clinical trial sites provided specimens that were well characterized by the site using Lyme-specific serological analyses, including EIA and/or Western Blot testing. In particular, specimens selected for the trial were required to have tested positive or indeterminate on a *B. burgdorferi* screening assay, typically an ELISA, in accordance with the two-tier testing protocol recommended by CDC/ASTPHLD (CDC (1995) "Recommendations for test performance and interpretation from the Second

National Conference on Serologic Diagnosis of Lyme Disease", Morbid. Mort. Weekly Rep. 44:590-591.).

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 dodecyl sulfate. 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 resolved *Borrelia burgdorferi* antigens are then reacted with diluted serum and controls (positive and negative sera of defined reactivity).

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 QualiCode™ *B. burgdorferi* IgM Western Blot Kit is an *in vitro* qualitative assay for the detection of human IgM antibodies reactive with *Borrelia burgdorferi* antigens present on a membrane strip. The QualiCode™ *B. burgdorferi* IgM Western Blot Kit is intended for supplemental testing of human serum specimens which yield positive or equivocal results on *B. burgdorferi* ELISA or IFA screening assays. QualiCode test results can provide additional, more specific evidence of infection with *B. burgdorferi* which may be useful in the diagnosis of Lyme disease.

The QualiCode™ *B. burgdorferi* IgM Western Blot Kit can be used to test human sera for IgM antibodies during the acute phase of disease, within one month of infection, in accordance with CDC/ASTPHLD guidelines. During this period, patients may not yet have developed a detectable IgG response. Beyond one month from infection, an IgG Western Blot test is recommended. Patients should not be tested solely for IgM

antibodies at this stage due to the higher probability of false-positive results. Symptomatic patients showing IgM but not IgG antibodies at an early stage in infection should be re-tested for IgG antibodies 2-4 weeks later.

6. Summary of Performance

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

Expected values

Three (3) investigational sites, including Immunetics and two (2) independent off-site investigators, assayed samples from the following patient populations:

1. Normal population (n=430) comprised of samples from Lyme disease endemic (n=279) and non-endemic (n=151) regions.

2. Cross – Reactive Panel (n=172) comprised of samples from patients with diseases other than Lyme disease that may be cross – reactive.

3. Lyme Disease Panel (n=186) comprised of samples from patients with a clinical diagnosis of Lyme disease, based on presence of erythema migrans or one or more symptoms of late Lyme disease, and which tested positive or equivocal on ELISA or other screening assays for *B. burgdorferi* antibodies.

Specificity

Specificity of the device was determined from analysis of results of testing normal donor specimens from endemic and non-endemic regions and potentially cross reactive disease specimens (602 total samples). The specificity values derived from testing each population are shown in the table below in the "% Negative" column:

Sample Type	n	% Positive	% Negative	95% CI
Normal – endemic region	279	5%	95%	92-97 %
Normal – non-endemic region	151	4%	96%	92-98 %
Normal - overall	430	4%	96%	93-97 %
Cross – Reactive Panel	172	13%	87%	88-96%

Sensitivity

Sensitivity of the device was determined by testing a total of 186 well-characterized sera from patients with Lyme disease, which had been drawn at different times after onset of disease. Sensitivity for each time after onset category is shown in the table below in the "% Positive" column:

Sensitivity of the Immunetics, Inc. QualiCode™ *B. burgdorferi* IgM Western Blot Kit vs. Time after Onset

Draw Time (months)	n	% Positive	% Negative	95% CI
Unknown	54	74%	26%	60-85 %
<1	76	91%	9%	82-96 %
1-2	23	83%	17%	61-94 %
3-12	16	63%	37%	35-82 %
>12	17	47%	53%	25-72 %

Reproducibility

Inter-lot reproducibility was determined by assaying a panel of 20 specimens, including positive, weakly reactive and negative sera, on three lots of the Immunetics QualiCode™ kit. There was 80% agreement between interpretations from the three kit lots. The reproducibility of scoring of individual bands between the three lots varied from 80% to 100%, averaging 88%.

Inter-run reproducibility was determined by assaying the 20 specimen panel twice, on separate days, at each of three sites. There was 85% agreement overall between interpretations from the two runs averaged over all three sites. The reproducibility of individual band scoring between the two runs averaged over all three sites varied between 75% and 93%, with an average of 85% over all three bands.

Inter-reader reproducibility was determined by assaying the 20 specimen panel twice, on separate days, at each of three sites, with each strip interpreted by two independent readers. There was 93% agreement overall between interpretations from the two readers averaged over the three sites. Band scoring reproducibility varied between 97% and 98% averaged over the three sites, with an average of 97% over all three bands.

Study	n	% Interpretation Agreement
Inter-lot	20	80
Inter-run	20	85
Inter-reader	20	93

7. 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.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 21 1999

Andrew E. Levin, Ph.D.
Scientific Director
Immunetics, Inc.
63 Rogers Street
Cambridge, Massachusetts 02142

Re: K991062
Trade Name: QualiCode™ *B. burgdorferi* IgM Western Blot Kit
Regulatory Class: II
Product Code: LSR
Dated: July 8, 1999
Received: July 9, 1999

Dear Dr. Levin:

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 legally marketed predicate 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.

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 Gutman

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

510(k) Number (if known): _____

Device Name: QualiCode *B. burgdorferi* IgM Western Blot Kit

Indications For Use:

The Immunetics QualiCode™ *B. burgdorferi* IgM Western Blot Kit 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 QualiCode™ *B. burgdorferi* IgM Western Blot Kit can be used to test human sera for IgM antibodies during the acute phase of disease, within one month of infection, in accordance with CDC/ASTPHLD guidelines. During this period, patients may not yet have developed a detectable IgG response. Beyond one month from infection, an IgG Western Blot test is recommended. Patients should not be tested solely for IgM antibodies at this stage due to the higher probability of false positive results. Symptomatic patients showing IgM but not IgG antibodies at an early stage in infection should be re-tested for IgG antibodies 2-4 weeks later.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991062

Prescription Use X OR Over-The-Counter Use ____
(Per 21 CFR 801.109)

(Optional format 1-2-96)