K040407

510(k) Summary

JUN 0 3 2004

Submitted by:

Immunetics, Inc.
27 Drydock Avenue
Boston, MA 02210-2377

Contact Person:

Andrew E. Levin, Ph.D.
President and CEO
617-896-9100

Date of Preparation:

February 13, 2003

Name and Address of Owner/Operator and Manufacturer

Immunetics, Inc.
27 Drydock Avenue
Boston, MA 02210-2377

Product Name

Trade Name: QuickELISA Anthrax-PA Kit

Common Name: *B. anthracis* QuickELISA Anthrax-PA™ Kit

Claim of Substantial Equivalence

The QuickELISA Anthrax-PA Kit is substantially equivalent to the Preamendments modified agar diffusion assay distributed by the U.S. Army Biological Laboratories since 1964. Both products utilize antigens to detect antibodies formed against *B. anthracis.*

Description

The Immunetics® QuickELISA Anthrax-PA Kit allows qualitative detection in human serum of total antibodies to the Protective Antigen (PA) protein of *B. anthracis*, in a non-subtype specific, non-species specific microwell ELISA† format. The PA toxin component of *B. anthracis* has been shown to elicit a detectable IgG response in naturally infected individuals and vaccine recipients‡. The assay is based on a single binding step, in which serum antibodies are incubated with a mixture of two rPA conjugates: Streptavidin-rPA and rPA-horseradish peroxidase (rPA-HRP). PA-specific, multivalent antibodies are able to form ternary

complexes in which streptavidin-rPA and rPA-HRP are bound to different antigen combining sites on a single antibody molecule. The complexes are bound to the biotin-coated microplate via the streptavidin conjugate and detected via the HRP conjugate.

In the assay procedure Sample Diluent, serum samples and Conjugate mixture are added to wells and incubated. Unbound antibodies and Conjugate are removed by wash steps, and bound anti-PA antibodies and HRP Conjugate are detected by adding a chromogenic peroxidase substrate containing tetramethylbenzidine (TMB). A blue product is produced in wells where antibody has been bound to the solid phase. The color development reaction is quenched by addition of an acidic Stop Solution, which causes a change in color from blue to yellow, after which optical Absorbance at 450nm corrected by 620-650nm background subtraction is measured in each well using an ELISA microplate reader. Turn-around time for the test is approximately 35 minutes if agitation is used, or 70 minutes without agitation. While the assay provides a qualitative result when undiluted samples are tested, it may also be used to obtain semi-quantitative anti-PA IgG titer results when serial dilution data are collected for the serum sample, in similar fashion to that described by U.S. Centers for Disease Control (CDC) Quinn, C.P. *et al.* Emerging Infectious Diseases 2002; 8(10):1103-1110.

Intended Use

The Immunetics® Quick ELISA Anthrax-PA Kit is intended for use in the presumptive detection of IgG and IgM antibodies to the Protective Antigen (PA) toxin protein of *B. anthracis* in human serum. The assay should only be used on serum samples from individuals with a clinical history, signs or symptoms consistent with anthrax infection; recipients of a licensed anthrax vaccine; or those with presumed contact with anthrax spores or vegetative bacilli. The diagnosis of anthrax infection must be made based on history, signs (such as raised bump skin infection with a characteristic black area that develops in the center), symptoms (such as fever or flu-like symptoms, non-productive cough, malaise, sore throat and/or regional lymphadenopathy) and when possible other laboratory data, in addition to the presence of antibodies to *B. anthracis* PA. Negative results in ELISA should not be used in isolation from other evidence to exclude anthrax infection.

Summary of Performance

1. Specificity

Table 1.1 Normal Human Sera, Agitated Incubations (Standard Protocol)

Test Method	# Tested	# FP	# TN	Specificity	95% Confidence
QuickELISA Anthrax-PA	583	5	578	99.14 %	98.01 – 99.72 %
CDC Anthrax-ELISA†	938	10	928	98.94 %	97.97 – 99.47 %

†NOTE: CDC *published results* (JEID 2002); archived data on unrelated samples

Table 1.2 Normal Human Sera, Agitated vs. Stationary Incubations

Incubation Type	# Tested	# FP	# TN	Specificity	95% Confidence
Stationary	100	0	100	100 %	96.38 – 100 %
Agitated	104	0	104	100 %	96.52 – 100 %

The specificity reported in the non-endemic normal population shown in Tables 1.1 and 1.2 above is performance data intended as background information, but does not necessarily represent specificity in the population of intended use.

2. Cross-Reactive Conditions

Table 2.1 Interference Study Summary, Agitated Incubations (Standard Protocol)

Test Protocol	# Tested	# FP	# TN	Specificity	95% Confidence
QuickELISA Anthrax-PA	225	1	224	99.56 %	97.55 – 99.99 %
CDC Anthrax-ELISA†	277‡	17‡	260‡	93.86%‡	90.46 – 96.38%‡

†NOTE: CDC *published results* (JEID 2002); archived data on unrelated samples

Table 2.2 Interference Study Results by Disease Condition

Interfering Condition	# Tested Samples	# FP	# TN	Specificity
ANA (anti-nuclear Ab)	21	0	21	100 %
EBV	20	0	20	100 %
HAV	4	0	4	100 %
HBV (HBsAg)	20	0	20	100 %
HIV	20	0	20	100 %
H. pylori	26	0	26	100 %
Influenza (patients)	10	0	10	100 %
Influenza (vaccinees)	20	0	20	100 %
Legionella	4	0	4	100 %
M. pneumoniae	20	0	20	100 %
SLE (lupus)	20	0	20	100 %
Rheumatoid Factor	20	0	20	100 %
RPR (syphilis)	20	1	19	95.0 %

3. Sensitivity

Table 3.1 Positive Serum Panels, Agitated Incubations (Standard Protocol)

AVA Vaccinees	**49**	**49**	**100 %**	**92.75 – 100 %**	**92.75 – 100 %**
All Patients	**34**	**19**	**100 %**	**89.72 – 100 %**	**82.35 – 100 %**
Cutaneous Anthrax	**18**	**13**	**100 %**	**81.47 – 100 %**	**75.29 – 100 %**
Inhalational Anthrax	**16**	**6**	**100 %**	**79.41 – 100 %**	**54.07 – 100 %**

Sensitivity in CDC PA IgG-specific ELISA = 100 % in all above groups

Sensitivity data on sera from recipients of anthrax vaccines other than AVA (Bioport Corporation, Lansing, MI) was not determined, and could potentially be different than that reported above in Table 3.1 for AVA recipients. Similarly, sensitivity data on sera from anthrax patients infected by the gastrointestinal exposure route was not determined, and could potentially be different than that reported above in Table 3.1 for patients infected by the cutaneous and inhalational exposure routes.

4. Analytical Sensitivity (A-SENS)

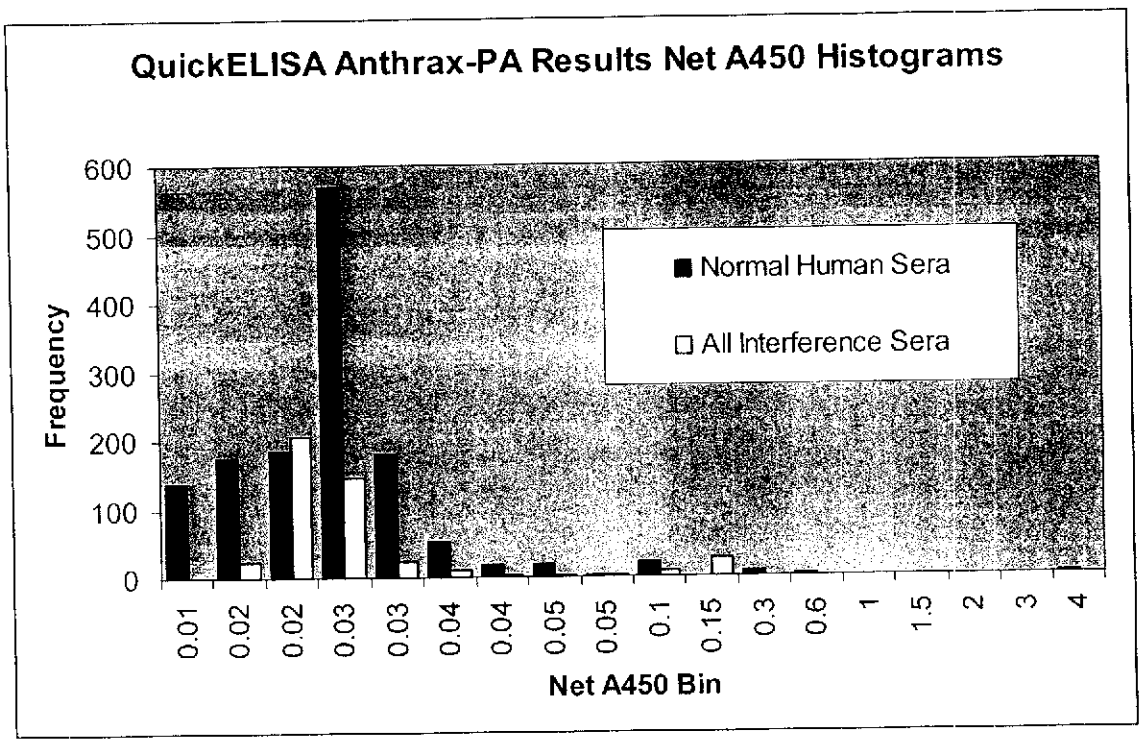
Table 4.1 PA IgG Reference Dilutions, Agitated Incubations (Std. Protocol)

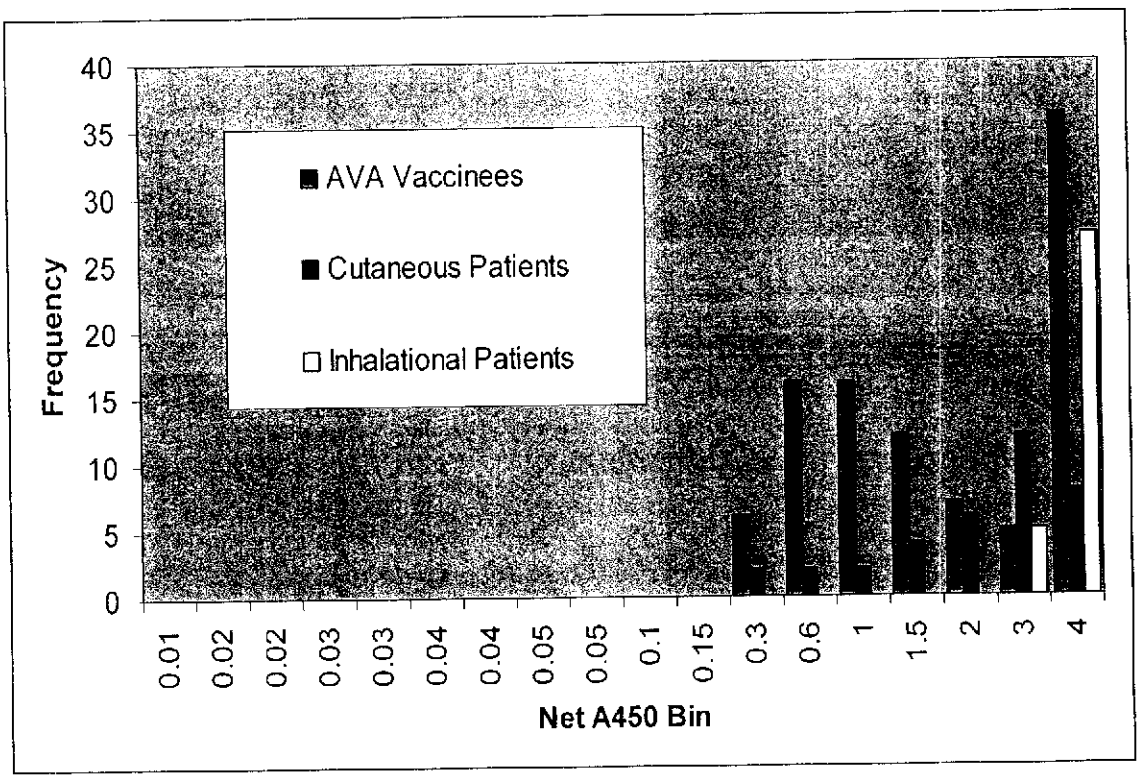
1000 ng/mL	**0.322**	**3.17**	0.3322	**0.3118**
500 ng/mL	**0.178**	**1.39**	0.1804	**0.1756**
250 ng/mL	**0.100**	**2.13**	0.1021	**0.0979**
125 ng/mL	**0.058**	**1.60**	0.0589	**0.0571**
62.5 ng/mL	**0.038**	**2.02**	0.0387	**0.0373**
31.3 ng/mL	**0.027**	**3.43**	0.0278	**0.0262**
15.6 ng/mL	**0.026**	**9.62**	**0.0329**	**0.0191**
0 ng/mL (NC)	**0.020**	**13.36**	**0.0222**	0.0178
LL-95%-C-INT (REF dilution) vs. UL-95%-C-INT (NC)				**≤ 31.3 ng/mL**
Best-fit 4-Parameter Curve Equation vs. Cutoff (Sensitivity @ Cutoff)				**229 ng/mL**

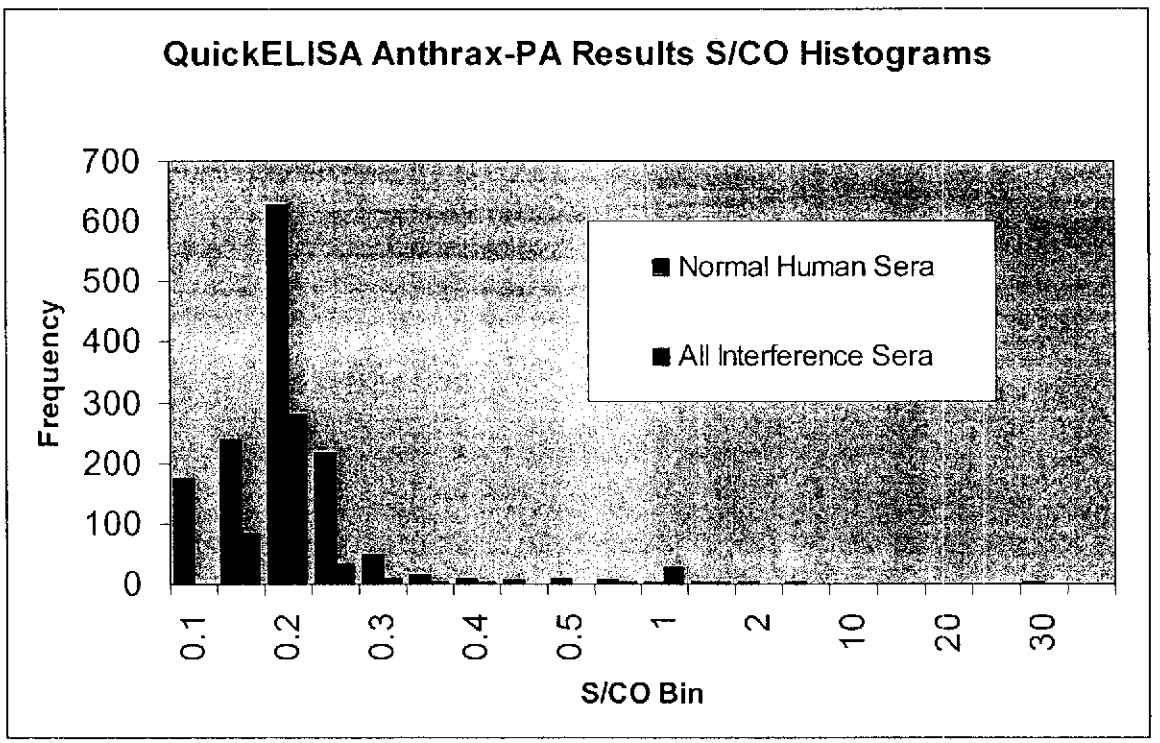
Assay Cutoff = 0.119
UL-95%-C-INT = Upper Limit of 95 % Confidence Interval
LL-95%-C-INT = Lower Limit of 95 % Confidence Interval

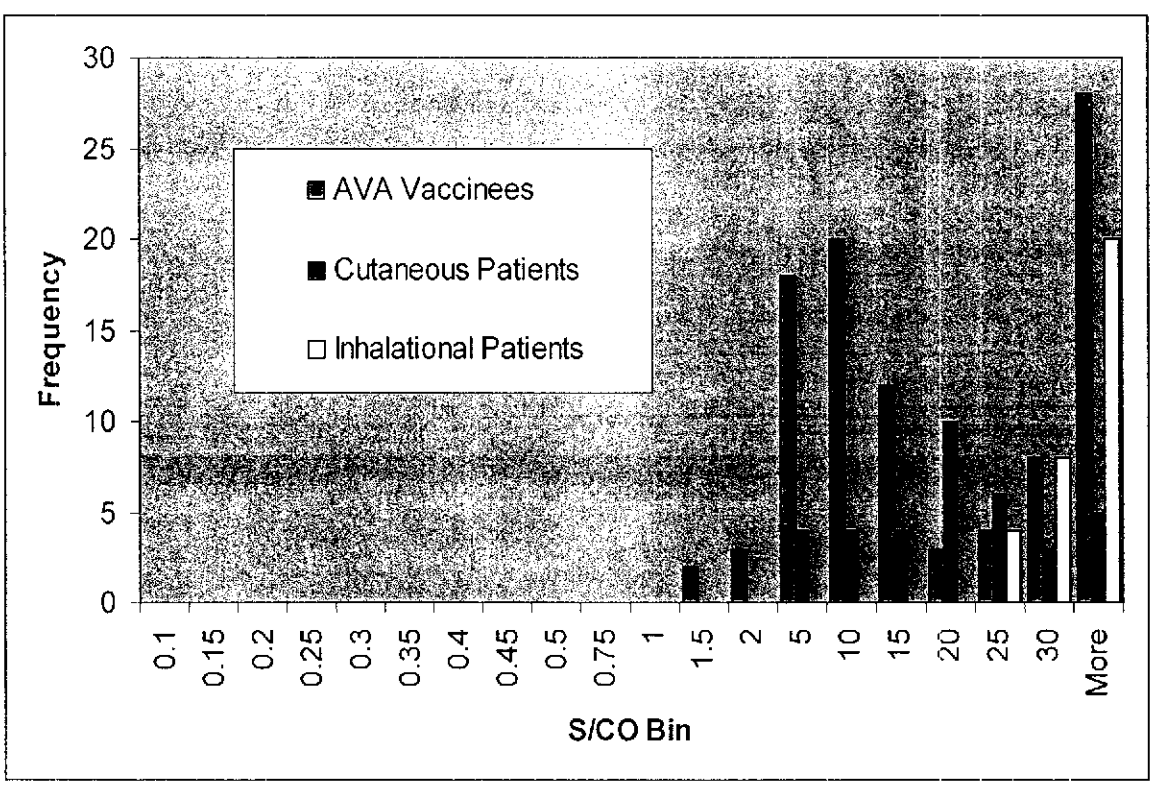
The 1.0µg/mL PA IgG Reference Sample (REF-1) used to establish Analytical Sensitivity was prepared from CDC standard serum pool designated AVR414 (described in JEID, 2002), and its activity was confirmed in a parallel serial dilution study against AVR414.

5. Specificity, Cross-Reactivity & Sensitivity Histogram Summary






QuickELISA Anthrax-PA Results S/CO Histograms
Frequency
700
600
500
400
300
200
100
0
Normal Human Sera
All Interference Sera
0.1
0.2
0.3
0.4
0.5
1
2
10
20
30
S/CO Bin


Frequency
30
25
20
15
10
5
0
AVA Vaccinees
Cutaneous Patients
Inhalational Patients
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
0.75
1
1.5
2
5
10
15
20
25
30
More
S/CO Bin

6. Reproducibility

Reproducibility was tested on a panel (n = 16) consisting of the kit controls (Low Positive Control, Positive Control and Negative Control); three strongly reactive (HiP1-HiP3, as shown below), one midrange reactive (MeP1) and three weakly reactive (LoP1-LoP3) positive samples; a 1.0 µg/mL PA IgG Reference Sample (REF-1), to confirm analytical sensitivity as ≤ 1 µg/mL; and five negative samples (N1-N5). Reproducibility testing was conducted for documentation of intra-assay, inter-assay, inter-site, inter-lot reproducibility and analytical sensitivity of the QuickELISA Anthrax-PA kit; the inter-lot reproducibility study results are shown in Table 6.1 below.

Table 6.1 Inter-Assay Reproducibility, Agitated Incubations (Standard Protocol)

PC	2.0	2.191	3.6	2.228	3.1	2.279	6.5
Low PC	1.5	0.850	3.6	0.854	3.1	0.875	5.5
[illegible]							
HiP1	0.4	3.794	7.0	3.810	6.4	3.824	5.3
HiP2	0.5	3.812	6.2	3.846	4.8	3.833	5.7
HiP3	2.0	3.870	5.1	3.720	5.7	3.829	4.8
LoP1	2.5	2.224	6.5	2.280	8.6	2.170	3.1
LoP2	3.0	0.604	11.0	0.629	10.4	0.594	2.2
LoP3	6.4	0.457	9.0	0.459	13.9	0.410	1.9
[illegible]							
REF-1	8.4	0.324	8.5	0.383	14.8	0.357	2.7
MeP1	7.8	2.944	7.7	2.968	10.1	2.575	2.4

Table 6.2 Inter-Lot Reproducibility, Agitated Incubations (Standard Protocol)

PC	11.2	2.565	1.9	2.736	4.6	2.191	3.6
Low PC	10.2	0.693	1.1	0.762	4.7	0.850	3.6
[illegible]							
HiP1	2.2	3.918	5.0	3.759	7.2	3.794	7.0
HiP2	0.9	3.745	5.9	3.781	5.4	3.812	6.2
HiP3	1.7	3.885	4.5	3.767	6.3	3.870	5.1
LoP1	22.6	1.410	12.6	1.777	10.9	2.224	6.5
LoP2	26.3	0.366	13.4	0.430	12.4	0.604	11.0
LoP3	20.5	0.314	10.7	0.341	13.3	0.457	9.0
[illegible]							
REF-1	15.7	0.238	12.7	0.269	11.9	0.324	8.5
MeP1	16.0	2.136	5.3	2.513	7.2	2.944	7.7

Conclusions

Based on the clinical performance results presented, this device has been shown to be safe and effective for the intended use in the presumptive detection of IgG and IgM antibodies to the Protective Antigen (PA) toxin protein of *B. anthracis* in human serum from vaccinated and unvaccinated populations.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 0 3 2004

Andrew E. Levin, Ph.D.
President and Chief Executive Officer
Immunetics, Inc.
27 Drydock Avenue
Boston, MA 02210-2377

Re: k040407
Trade/Device Name: QuickELISA Anthrax-PA™ Kit
Regulation Number: Unclassified
Product Code: NRL
Dated: May 25, 2004
Received: May 27, 2004

Dear Dr. Levin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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.

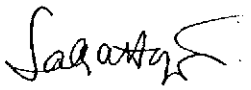
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K040407

Device Name: QuickELISA Anthrax-PA™ Kit

Indications For Use:

The Immunetics® QuickELISA™ Anthrax-PA Kit is intended for use in the qualitative detection of antibodies to the Protective Antigen (PA) protein of *B. anthracis* in human serum. The assay should be used only on serum samples from individuals with a clinical history, signs or symptoms consistent with anthrax infection as an aid in the diagnosis of anthrax, or from recipients of anthrax vaccine.

- The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and when possible other laboratory data, in addition to the presence of antibodies to *B. anthracis* PA. Negative results in ELISA should not be used in isolation from other evidence to exclude anthrax.
- The assay has not been evaluated in individuals without clinical signs or symptoms who were presumed exposed and who subsequently developed cutaneous or inhalation anthrax. There is no information available to interpret the meaning of a positive or negative test result for such individuals
- The assay has not been evaluated with specimens from patients infected by the gastrointestinal route; expected results with such infections are unknown.
- The minimum level of anti-PA antibodies that confers protection following vaccination is not known. The QuickElisa measures total antibody and the relationship between this value and protective immunity has not been established.
- The affinity and/or avidity of anti-PA IgG and IgM for the rPA antigen have not been determined with this assay.

Prescription Use __X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Division Sign-Off
Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K040407