Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device Generic Name: Reagent system for the measurement of antibodies against hepatitis B surface antigen

Device Trade Name: IMMULITE® Anti-HBs
IMMULITE® 2000 Anti-HBs

Applicant's Name and Address: Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045-5597

Premarket Approval Application (PMA) Number: P010052

Date of Panel Recommendation: None

Date of Notice of Approval to the Applicant: July 22, 2002

II. INDICATIONS FOR USE

IMMULITE Anti-HBs

For *in vitro* diagnostic use with the IMMULITE automated immunoassay analyzer for the qualitative measurement of total antibodies to the hepatitis B surface antigen (anti-HBs) in human serum and plasma (heparinized or EDTA). Assay results may be used as an aid in the determination of susceptibility to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination, or where vaccination status is unknown. Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown. The detection of anti-HBs is indicative of laboratory diagnosis of seroconversion from hepatitis B virus (HBV) infection.

IMMULITE 2000 Anti-HBs

For *in vitro* diagnostic use with the IMMULITE 2000 automated immunoassay analyzer for the qualitative measurement of total antibodies to the hepatitis B surface antigen (anti-HBs) in human serum and plasma (heparinized or EDTA). Assay results may be used as an aid in the determination of susceptibility to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination, or where vaccination status is unknown. Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown. The detection of anti-HBs is indicative of laboratory diagnosis of seroconversion from hepatitis B virus (HBV) infection.

III. DEVICE DESCRIPTION

The IMMULITE and IMMULITE 2000 Anti-HBs kits are the subjects of this PMA. Data are presented separately for each assay. Each assay has its own package insert.

The IMMULITE and IMMULITE 2000 Anti-HBs kits are solid phase, two step chemiluminescent enzyme immunoassays designed for use on the automated IMMULITE and IMMULITE 2000 analyzers, for the qualitative measurement of *antibodies against hepatitis B surface antigen* (HBsAg) in human serum or plasma. The kits are intended for *in vitro* use as an aid in the determination of immune status to the hepatitis B virus.

The kits' solid phase is a polystyrene bead coated with purified HBsAg subtypes ad and ay. The patient sample and a protein-based buffer are simultaneously introduced into the Test Unit and incubated for approximately 30 minutes at 37 ^{o}C with intermittent agitation. During this time, antibodies to HBsAg in the patient sample bind to the HBsAg-coated bead. Unbound serum is then removed by a centrifugal wash. An alkaline phosphatase-labeled HBsAg is introduced, and the reaction tube is incubated with agitation for another 30 minute cycle. The unbound enzyme conjugate is removed by a centrifugal wash. After the wash, a chemiluminescent substrate is added, and the reaction tube is incubated with agitation for a further 5 – 10 minutes.

The chemiluminescent substrate is a phosphate ester of adamantyl dioxetane which undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light. The bound complex and the resulting photon output, measured as cps by the photomultiplier tube, are related to the presence of antibodies to HBsAg in the sample.

IV. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

There are no known contraindications for the IMMULITE Anti-HBs and IMMULITE 2000 Anti-HBs Immunoassay.

Warnings and precautions for the IMMULITE Anti-HBs and IMMULITE 2000 Anti-HBs Immunoassays are stated in the device labeling.

V.   ALTERNATIVE PRACTICES OR PROCEDURES

Measuring antibodies against hepatitis B surface antigen in individuals may be achieved by using a variety of commercially available, FDA licensed or approved serological tests. Assays have been developed using radioimmunoassay or enzyme immunoassay methodologies. When the test results are used in combination with other serological markers expressed during the three phases of incubation, the presence of hepatitis B virus may be determined.

VI.   MARKETING HISTORY

IMMULITE Anti-HBs and IMMULITE 2000 Anti-HBs have been marketed internationally as an aid in the determination of acute and chronic hepatitis B virus infection since July 1996. IMMULITE and IMMULITE 2000 Anti-HBs have received European Union CE Mark approval and have been marketed in Europe since June 2001. The devices have not been withdrawn from any country for reasons related to safety and effectiveness.

VII. POTENTIAL ADVERSE EFFECTS OF DEVICE ON HEALTH

As an *in vitro* diagnostic test system, there is no direct adverse effect of IMMULITE and IMMULITE 2000 Anti-HBs assays on the health of the patient. The possibility of erroneous test results due to test malfunctions or operator errors exists. A false non-reactive result would make the patients unnecessarily receive a vaccine, vaccine booster, hyperimmune globulin, or be considered not to have recovered from an HBV infection when in fact they have recovered.

A false reactive test result may be of concern to patients or the public health because the patient is considered to be immune to natural HBV infection or was successfully vaccinated. In this case, the risk is that the patient would not receive a vaccine, vaccine booster, or hyperimmune globulin, and would be at higher risk of infection if exposed to HBV. Once exposed, the risk of this patient spreading infection to uninfected or non-immune members of the community increases.

Blood specimens obtained from a subject infected with hepatitis B prior to the appearance of an antibody titer have the potential to misdiagnose the patient as not being infected. Additionally, specimens obtained after the disappearance of anti-HBc IgM antibodies, in the absence of test results for other hepatitis B markers, may lead to misdiagnosis of a hepatitis B infected patient.

The risk of incorrect test results is inherent with all *in vitro* diagnostic products. Therefore, the above potential risks are not unusual in the laboratory setting. Appropriate warnings for each of these risks are contained in the labeling and package insert

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instructions. Standard good laboratory practices are considered sufficient to minimize risks to the end user.

VIII. SUMMARY OF NON CLINICAL STUDIES

Analytical Specificity

Analytical specificity was evaluated at two clinical sites in the United States and one European site. In the United States, serum specimens from 17 subgroups of patients with potentially cross-reacting microorganisms or conditions were tested by IMMULITE Anti-HBs, IMMULITE 2000 Anti-HBs, and a commercially available enzyme immunoassay for anti-HBs (Kit A), and the results are listed in the package insert.

In the European study, six specimens from *H. pylori* positive patients, four from antinuclear antibody (ANA) positive patients, and 27 from patients with positive rheumatoid factor (RF) were tested by IMMULITE Anti-HBs. IMMULITE Anti-HBs test results were negative for all six *H. pylori* specimens, negative for 3/4 ANA specimens, and negative for 24/27 RF specimens.

In the European study, six specimens from *H. pylori* positive patients, three from antinuclear antibody (ANA) positive patients, and 26 from patients with positive rheumatoid factor (RF) were tested by IMMULITE 2000 Anti-HBs. IMMULITE 2000 Anti-HBs test results were negative for all six *H. pylori* specimens and all three ANA specimens.

IMMULITE 2000 Anti-HBs results were negative for 23/26 and positive for 3/26 RF specimens.

Effects of Bilirubin, Lipemia and Hemolysis

To simulate moderate and severe icterus, different volumes of each of 5 patient samples ranging from negative to high positive total antibodies against hepatitis B surface antigen were pipetted into lyophilized unconjugated bilirubin to achieve 3 levels of bilirubin concentrations (10, 20 and 40 mg/dL) for each sample. The spiked and unspiked samples were assayed by the IMMULITE and IMMULITE 2000 Anti-HBs assays. In the IMMULITE Anti-HBs tests, the spiked samples had averages of 98%, 90% and 85% recovery for all samples for 10, 20 and 40 mg/dL bilirubin concentrations, respectively. In the IMMULITE 2000 Anti-HBs tests, the spiked samples had averages of 96%, 97% and 95% recovery for all samples for 10, 20 and 40 mg/dL bilirubin concentrations, respectively. This study demonstrated that the measurement of antibodies against hepatitis B surface antigen was not affected by the presence of bilirubin up to 40 mg/dL.

To simulate mild, moderate and severe hemolysis, the same five samples were spiked with hemolysate to achieve final hemoglobin levels of 168, 252 and 504 mg/dL. The samples were assayed, both spiked and unspiked, by the IMMULITE and IMMULITE 2000 Anti-HBs assays. In both the IMMULITE and IMMULITE 2000 Anti-HBs tests,

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the low samples had significant increases in the antibodies against hepatitis B surface antigen when spiked with hemolysate. It was concluded that the measurement of antibodies against hepatitis B surface antigen may be affected by the presence of red blood cells. The results of hemolyzed samples should be interpreted with caution.

The same 6 samples were each spiked with 4 levels of triglycerides at 500, 1000, 2000 and 3000 mg/dL to evaluate the effect of lipemia on the IMMULITE and IMMULITE 2000 Anti-HBs assays. Unspiked and spiked samples were tested by the IMMULITE and IMMULITE 2000 Anti-HBs assays. Since no significant increases of antibody levels were observed in the spiked samples with the increase of triglyceride levels, it was concluded that the measurement of antibodies to hepatitis surface antigen was not affected by the presence of lipemia (triglycerides up to 3000 mg/dL).

Hook Effect and Carryover

The hook effect study demonstrated that the IMMULITE and IMMULITE 2000 Anti-HBs assays did not have a hook effect up to at least 10,000 mIU/mL.

The carryover study demonstrated that the IMMULITE and IMMULITE 2000 Anti-HBs assays did not exhibit a carryover phenomenon when samples were preceded by a sample with a very high titer of antibodies against hepatitis B surface antigen.

Interfering Substances

A study was conducted to evaluate the effects of interfering substances on IMMULITE and IMMULITE 2000 Anti-HBs assays. Potential interfering substances that included common serum constituents, chemotherapeutic and other drugs were spiked into serum samples with 5 or 6 different levels of anti-HBs. Listed below are the substances and their test levels (concentration).

Interferring Substance	Concentration
HUMAN ALBUMIN	6 g/dL
ASCORBIC ACID	3 mg/dL
ALT	7000 U/L
AST	7000 U/L
ALK PHOSPHATASE	5000 U/L
CORTISONE	400 ug/dL
CYCLOSPORIN A	18.02 ug/dL
GANCICLOVIR	11.8 ug/mL
ETHANOL	350 mg/dL
INTRON A	2730 IU/mL
LAMIVUDINE	20 ug/mL
LDH	6000 U/L
NELFINAVIR	40 ug/mL

This study demonstrated that the measurement of antibodies against hepatitis B surface antigen by IMMULITE and IMMULITE 2000 Anti-HBs was not affected by the presence of any of the interfering substances listed up to the levels tested.

Effects of Anticoagulants

The measurement of specimens is not affected by the presence of heparin and EDTA anti-coagulants, as shown in a study that included 46 specimens collected into plain, heparinized and EDTA vacutainer tubes. By regression:

IMMULITE Anti-HBs

(Heparin) = 1.04 (Serum) + 10 mIU/mL   r = 0.97
(EDTA) = 1.11 (Serum) – 2 mIU/mL r = 0.93
Around the cutoff (10 mIU/mL), heparinized specimens demonstrated a 112% recovery and EDTA specimens demonstrated a 103% recovery. This may indicate that with heparin and EDTA, there could be false positives around the cut-off.

IMMULITE 2000 Anti-HBs

 (Heparin) = 1.03 (Serum) + 14 mIU/mL r = 0.97
(EDTA) = 1.05 (Serum) + 16 mIU/mL r = 0.88
Around the cutoff (10 mIU/mL), heparinized specimens demonstrated a 117% recovery and EDTA specimens demonstrated a 106% recovery. This may indicate that with heparin and EDTA, there could be false positives around the cut-off.

Precision

Precision studies for the IMMULITE and IMMULITE 2000 Anti-HBs assays were conducted at three sites. Included in the studies were three controls and nine patient samples covering the entire working range (3 – 2000 mIU/mL) of both assays. All controls and serum samples were assayed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates at 3 US sites. The IMMULITE Anti-HBs assay was tested for three lots and at three sites.

Results by IMMULITE and IMMULITE 2000 Anti-HBs are expressed in mIU/mL. Statistics including the means, standard deviations, the intraassay and total precision were calculated for samples 2 through 8. Statistics for samples 1 and 9 were not calculated because they consistently yielded results less than 3 mIU/mL and results greater than 2000 mIU/mL, respectively. The IMMULITE and IMMULITE 2000 Anti-HBs lot-to-lot precision data and the IMMULITE Anti-HBs site-to-site precision data are also provided. The IMMULITE 2000 Anti-HBs lot-to-lot precision has not been evaluated. Because the lot-to-lot precision of the assay had previously been established, and the Stability studies included three lots, no additional data was required.

IMMULITE Anti-HBs Intra-assay and Total Precision (mIU/mL), IMMULITE 2000 Anti-HBs Intra-assay and Total Precision (mIU/mL), IMMULITE Anti-HBs Lot-to-Lot and Site-to-Site Precision, and IMMULITE 2000 Anti-HBs Site-to-Site Precision data for Site 1, Site 2, and Site 3 are included in the package insert.

EDTA and heparinized samples were assayed in duplicate in three runs on three days at three U.S. sites for three lots of IMMULITE Anti-HBs and one lot of IMMULITE 2000 Anti-HBs. The median total variance of coefficients (EDTA, 4.2%; heparin, 4.5%) demonstrated that these alternative sample types do not affect the precision of IMMULITE and IMMULITE 2000 Anti-HBs.

Stability

Stability studies for IMMULITE and IMMULITE 2000 Anti-HBs were conducted by using 3 lots of IMMULITE Anti-HBs, and one lot of IMMULITE 2000 Anti-HBs. The kits and components were subjected to different storage/stress conditions to simulate adverse conditions that might be encountered during shipment and use at clinical laboratories, to establish the long-term (shelf-life) claims, to approximate and support the real time stability and to test the robustness of individual components.

The studies demonstrated that the performance of IMMULITE and IMMULITE 2000 Anti-HBs assays was not affected if properly stored at package insert conditions for at least 720 days.

These studies also demonstrated that the performance of IMMULITE and IMMULITE 2000 Anti-HBs assays was not affected following initial stresses (37°C, or –20°C) for at least 720 days.

IX. SUMMARY OF CLINICAL STUDIES

Expected Values

Individuals acutely infected with the hepatitis B virus will exhibit anti-HBs approximately two weeks after the disappearance of HBsAg. This antibody response will reach peak levels after several months and gradually decline over a period of years. The majority of persons who have been vaccinated against HBV will also have detectable levels of anti-HBs.

Demographics and expected prevalence rates for different categories of subjects, (Apparently Healthy individuals, HBV Acute Patients, and HBV Chronic Patients), each of whom provided one specimen, were obtained from four clinical studies. The sites were: one in the northwestern United States (Study 1), two in the southern United States (Study 3 using specimens from China and Study 4), and one in Europe, are summarized in the package inserts. Some individuals were characterized as at high risk or low risk of exposure to hepatitis B.

Clinical Studies

A total of 769 subjects were tested, using FDA-approved or licensed hepatitis B assays (Reference markers), at four clinical sites, to assess the performance of the IMMULITE Anti-HBs and IMMULITE 2000 Anti-HBs assays. Only initial test results are reported.

The data were analyzed following the assignment of specimen classification based upon the reactive(+)/ nonreactive(-) patterns for the HBV reference serological markers. Specimen classification was based only on the HBV serological marker results for that particular specimen. No other laboratory or clinical information was used in the disease classification process.

Site 1: Conducted in the northwestern United States, this study included 281 patients, consisting of 138 males and 88 females. Gender for 55 subjects was not reported. These subjects had an average age of 43 years, ranging from 21 to 85 years. Distributions of the ethnicity of the subjects are shown in the following table.

Ethnicity	N	%
African American	15	5.3%
Caucasian	169	60.1%
Hispanic	2	0.7%
Asian	32	11.4%
Other	3	1.1%
Unknown	60	21.4%
Total	281	100.0%

These subjects included acute and chronic hepatitis B patients, vaccinated individuals, pregnant women, and apparently healthy individuals, and patients with potentially crossreactive substances and medical conditions.

A total of 281 specimens were prospectively (n=92) and retrospectively (n=189) collected and tested by FDA-approved or licensed hepatitis B assays for six HBV serological markers (HBsAg, Anti-HBc, Anti-HBs, Anti-HBc IgM, HBeAg, and Anti-HBe). Characterization based on single point specimens by the reference serological markers demonstrated 17 unique patterns:

Characterization based on single point specimens	Number of patients	HBV Reference Markers					
		HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	2	+	–	–	–	–	–
Acute	1	+	+	–	–	–	–
Acute	32	+	–	+/-	+	+	–
Acute	34	+	+	+/-	+	–	–
Chronic	2	+	–	–	+	–	–
Chronic	3	+	+/-	–	+	+	+
Chronic	1	+	–	–	+	–	+
Chronic	1	+	+	+/-	+	–	+
Early Recovery	16	–	–	+/-	+	+	+
Early Recovery	4	–	–	–	+	+	–
Early Recovery	19	–	–	–	+	+/-	–
Early Recovery	1	–	–	+	+	+/-	+
HBV vaccine response	27	–	–	–	–	–	+
Not previously infected	120	–	–	–	–	–	–
Recovered	16	–	–	–	+/-	–	+
Recovered	1	–	+/-	–	+	–	+
Uninterpretable	1	–	+	–	–	–	–

Based on the above classifications the IMMULITE and IMMULITE 2000 Anti-HBs results were compared to Kit A, a reference assay for the determination of anti-HBs.

For the IMMULITE Anti-HBs the combined Total Positive agreement is 92.4% (61/66) with a 95% CI of 83.2 to 97.5%. The Negative agreement is 97.2% (209/215) with a 95% CI of 94.0 to 99.0%. The combined Total agreement is 96.1% (270/281) with a 95% CI of 93.1 to 98.0%.

For the IMMULITE 2000 Anti-HBs the combined Total Positive agreement is 90.9% (60/66) with a 95% CI of 81.3 to 96.6%. The Negative agreement is 96.3% (207/215) with a 95% CI of 92.8 to 98.4%. The combined Total agreement is 95.0% (267/281) with a 95% CI of 91.8 to 97.3%.

Site 2: Conducted in the northeastern United States, this study included 209 patients, consisting of 104 males and 103 females. Gender for two patients was not reported. These patients had an average age of 47 years, ranging from newborn to 93 years. Distributions of the ethnicity of the patients are shown in the following table.

Ethnicity	N	%
African American	21	10.0%
Caucasian	101	48.3%
Hispanic	3	1.4%
Asian	6	2.9%
Other	7	3.3%
Unknown	71	34.0%
Total	209	100.0%

Included were patients with potentially crossreactive substances and medical conditions. A total of 209 retrospective specimens were collected and tested by FDA-approved or licensed hepatitis B assays for four HBV serological markers (HBsAg, Anti-HBc IgM, Anti-HBc, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated eight unique patterns:

Characterization based on single point specimens	No. of patients	HBV Reference Markers			
		HBsAg	Anti-HBc IgM	Anti-HBc	Anti-HBs
Acute	8	+	–	–	–
Acute	9	+	+/-	+	–
Chronic	2	+	–	+	+
Early recovery	33	–	+/-	+	+
Early recovery	17	–	–	+	–
HBV vaccine response	32	–	–	–	+
Not previously infected	107	–	–	–	–
Uninterpretable	1	+	–	–	+

Based on the above classifications the IMMULITE and IMMULITE 2000 Anti-HBs results were compared to Kit A.

For the IMMULITE Anti-HBs the combined Total Positive agreement is 94.1% (64/68) with a 95% CI of 85.6 to 98.4%. The Negative agreement is 95.0% (134/141) with a 95% CI of 90.0 to 98.0%. The combined Total agreement is 94.7% (198/209) with a 95% CI of 90.8 to 97.3%.

For the IMMULITE 2000 Anti-HBs the combined Total Positive agreement is 94.1% (64/68) with a 95% CI of 85.6 to 98.4%. The Negative agreement is 97.2% (137/141) with a 95% CI of 92.9 to 99.2%. The combined Total agreement is 96.2% (201/209) with a 95% CI = 92.6 to 98.3%.

Site 3: Specimens obtained from China were tested in the southern United States, this study included 79 patients and was comprised of 13 females and 55 males (gender for 11 patients was not reported) with an average age of 36 years, ranging from 18 to 82 years. These were prospectively recruited patients from a clinically well-characterized, homogeneous population: acute hepatitis B patients who presented with symptoms typical of acute hepatitis B such as jaundice, persistent fatigue, loss of appetite, pale stools and liver enlargement. Their ALT and AST results were significantly elevated at the time of diagnosis.

A total of 79 specimens were prospectively collected and tested by FDA-approved or licensed hepatitis B assays for six HBV serological markers (HBsAg, HBeAg, Anti-HBc IgM, Anti-HBc, Anti-HBeAg, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated 11 unique patterns:

Characterization based on single point specimens	Number of patients	HBV Reference Markers					
		HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	23	+	–	+/-	+	+	–
Acute	8	+	+/-	+	+	+	–
Acute	1	+	–	+	+/-	–	–
Acute	35	+	+	+/-	+	–	–
Acute	4	+	+	+	+	–	+/-
Chronic	1	+	–	–	+	–	–
Chronic	3	+	+/-	–	+	+	–
Chronic	1	+	+	+/-	+	–	+
Chronic	1	+	+	+	+	+	+
Recovered	1	–	–	–	+/-	–	+
Uninterpretable	1	+	–	+	+	+	+

Based on the above classifications the IMMULITE and IMMULITE 2000 Anti-HBs results were compared to Kit A.

For the IMMULITE Anti-HBs the combined Total Positive agreement is 25.0% (2/8) with a 95% CI of 3.2 to 65.1%. The Negative agreement is 98.6% (70/71) with a 95% CI of 92.4 to 100.0%. The combined Total agreement is 91.1% (72/79) with a 95% CI of 82.6 to 96.4%.

For the IMMULITE 2000 Anti-HBs the combined Total Positive agreement is 12.5% (1/8) with a 95% CI of 0.0 to 52.7%. The Negative agreement is 98.6% (70/71) with a 95% CI of 92.4 to 100.0%. The combined Total agreement is 89.9% (71/79) with a 95% CI of 81.0 to 95.5%.

Site 4: Conducted in the southern United States, this study included retrospectively collected specimens from 200 pregnant subjects. These subjects had an average age of 28 years, ranging from 17 to 41 years.

A total of 200 specimens were tested by FDA-approved or licensed hepatitis B assays for four HBV serological markers (HBsAg, Anti-HBc IgM, Anti-HBc, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated three unique patterns:

Characterization based on single point specimens	Number of subjects	HBV Reference Markers			
		HBsAg	Anti-HBc IgM	Anti-HBc	Anti-HBs
Early recovery	4	–	+/-	+	+
Early recovery	2	–	–	+	–
HBV vaccine response	42	–	–	–	+
Not previously infected	152*	–	–	–	–

Based on the above classifications the IMMULITE and IMMULITE 2000 Anti-HBs results were compared to Kit A. (Note: One specimen was not tested for IMMULITE Anti-HBs or for the IMMULITE 2000 Anti-HBs.)

For the IMMULITE Anti-HBs the combined Total Positive agreement is 100.0% (46/46) with a 95% CI of 92.3 to 100.0%. The Negative agreement is 98.7% (151/153) with a 95% CI of 95.4 to 99.8%. The combined Total agreement is 99.0% (197/199) with a 95% CI of 96.4 to 99.9%.

For the IMMULITE 2000 Anti-HBs the combined Total Positive agreement is 100% (46/46) with a 95% CI of 92.3 to 100%. The Negative agreement is 98.7% (151/153) 95% CI of 95.4 to 99.8%. The combined Total agreement is 99.0% (197/199) 95% CI of 96.4 to 99.9%.

X. CONCLUSIONS DRAWN FROM STUDIES

The studies conducted demonstrated that when used according to the instructions for use, the IMMULITE Anti-HBs and the IMMULITE 2000 Anti-HBs has:

- Comparable performance when testing specimens collected in serum and plasma (heparin or EDTA).

- Stability for 720 days without loss of activity when stored under recommended conditions.

- Precision at estimates of <7% intra-assay, <21% site-to-site and <13% lot-to-lot.

- Minimal cross-reactivity with antibodies to various infections agents when compared to the reference assay.

- The ability to measure antibodies against hepatitis surface antigen in human serum or plasma. The results indicated a clinical sensitivity and specificity that correlate well to a commercially available reference assay.

Safety

As a diagnostic test, the anti-HBsAg assay involves removal of blood from an individual for testing purposes. The test, therefore, presents no more safety hazard to an individual being tested than other tests where blood is removed.

Benefit/Risk Analysis

The PMA studies provide reasonable assurance that support that assay results may be used:

- As an aid in the determination of susceptibility to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination, or where vaccination status is unknown.
- Along with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection.
- To allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis when etiology is unknown.
- As an indication of seroconversion from hepatitis B virus (HBV) infection.

The potential risks seen for these *in vitro* diagnostic tests are not unusual in the laboratory setting, and appropriate warnings for these risks are contained in the labeling and package insert instructions for these devices. Standard good laboratory practices are considered sufficient to minimize the risks to the end user.

The benefits to HBV-infected individuals tested by these devices outweigh any potential adverse event or risk to the patient or user due to device malfunction or operator error.

XI. PANEL RECOMMENDATIONS

Pursuant to Section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Microbiology Devices Advisory Panel meeting because the information in the PMA substantially duplicated information previously reviewed by this Panel.

XII. CDRH DECISION

FDA issued an approval order on July 22, 2002.

The applicant's manufacturing facility was found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIII. APPROVAL SPECIFICATIONS

Directions for Use: See labeling

Hazards to Health from Use of the Device: See Contraindications, Warnings, Precautions and Adverse Events in the labeling**.**

Postapproval Requirements and Restrictions: See approval order.