MAY 14 1999

510(K) SUMMARY
FOR THE
BAYER IMMUNO 1™ CA 125 II™ ASSAY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: ____K983715_____

1. GENERAL INFORMATION

Trade Name: Bayer Immuno 1™ CA 125 II™ Assay

Classification Name: Tumor-Associated Antigen Immunological Test Systems

Gabriel J. Muraca, Jr.

4/12/99

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Date

This premarket notification is to expand the intended use of the Immuno 1 CA 125 II™ Assay to include management (monitoring) of ovarian cancer patients. The Bayer Immuno 1™ CA 125 II™ Assay received 510(k) clearance (K964098) on October 31, 1997 with the intended use as an indication for second look diagnostic procedures in ovarian cancer patients. This intended use was supported with clinical data demonstrating assay values in the target ovarian cancer population as well as expected values in healthy individuals and patients with related benign and malignant diseases. The 510(k) referenced above also reported non-clinical laboratory studies including reagent characterization, analytical sensitivity, imprecision, assay specificity and interfering substances, linear range, sample dilution, hook effect, reagent lot-to-lot variation, and method comparison to the Centocor CA 125 II™ RIA. In this current 510(k) application, the performance and clinical safety and effectiveness of the Bayer Immuno 1™ CA 125 II ™ Assay for the management (monitoring) of ovarian cancer patients has been established by external clinical studies in the target population of longitudinal ovarian cancer patients and by comparison to accepted diagnostic procedures in accordance with the "Guidance Document For Submission of Tumor Associated Antigen Premarket Notifications, 510(k), to the FDA." Clinical evaluations of the Bayer Immuno 1™ CA 125 II™ Assay at two US clinical trial sites demonstrated clinical safety and effectiveness. These studies validated clinical performance characteristics and the comparison to accepted diagnostic procedures.

2. INDICATIONS FOR USE

The Bayer Immuno 1™ CA 125 II™ Assay is an *in vitro* device for the quantitative measurement of OC 125 reactive determinants associated with a high molecular weight glycoprotein in serum of women with primary epithelial invasive ovarian cancer. The Bayer Immuno 1™ CA 125 II™ Assay is indicated as an aid in the management (monitoring) of ovarian cancer patients when used in conjunction with other diagnostic procedures. The CA 125 II™ Assay is also indicated as a one time test for use as an aid in the detection of residual ovarian carcinoma in patients who have undergone first line therapy and would be considered for diagnostic second look procedures. An assay value of greater than or equal to 35 U/mL is predictive of residual disease, provided that alternative causes of an elevated CA 125 II™ assay value can be excluded. It is recommended that the *Bayer Immuno 1 CA 125 II* assay be used under the order of a physician trained and experienced in management of gynecological cancers.

3. DEVICE DESCRIPTION

The Bayer Immuno 1™ CA 125 II™ Assay utilizes a well-established immunoassay technology in which one monoclonal antibody (M11) is conjugated to fluorescein (R1) and a second monoclonal antibody (OC 125) is conjugated to alkaline phosphatase (R2). An Immuno 1 Magnetic Particle coated with anti-fluorescein antibody, the R1 conjugate, and patient sample, calibrator, or control are mixed simultaneously and incubated at 37°C on the system. The R2 conjugate is then added, and binds to the immobilized CA 125 to form a sandwich immunocomplex on the solid phase. The magnetic particles complexed with the immunological sandwich are then washed to separate unbound molecules, and a colorimetric substrate is added. The rate of conversion of substrate to a compound with absorbance at 405 or 450 nm is measured; the measured rate is proportional to the concentration of CA 125 antigen in the sample. A cubic-through-zero curve fitting algorithm is used to generate standard curves.

The assay has a range of 0 to 500 U/mL. The Bayer Immuno 1™ CA 125 II™ Assay Calibrators consist of a set of six calibrator levels at 0, 15, 30, 80, 200, and 500 U/mL.

4. SUMMARY OF STUDIES

The Bayer Immuno 1™ CA125 II™ Assay received 510(k) clearance (K964098) on October 31, 1997 with the intended use as an indication for second look diagnostic procedures in ovarian cancer patients. This intended use was supported with clinical data demonstrating assay values in the target ovarian cancer population as well as expected values in healthy individuals and patients with related benign and malignant diseases. In addition, the Immuno 1 CA 125 II™ Assay was evaluated at three clinical sites for imprecision: Site 1 was Bayer Corporation, Tarrytown, NY, Site 2 was Helsinki University Central Hospital, Finland and Site 3 was Hôpital Saint-Luc, Montreal. The 510(k) referenced above also reported non-clinical laboratory studies performed at Bayer Corporation, Diagnostics Division, Tarrytown, New York. These studies included reagent characterization, analytical sensitivity, imprecision, assay specificity and interfering substances, linear range, parallelism (sample dilution), hook effect, reagent lot-to-lot variation, and method comparison to the Centocor CA 125 II RIA.

The clinical evaluation of Immuno 1 CA 125 II™ Assay as a quantitative measure of OC 125 reactive determinants in human serum for use as an adjunctive test in the management of ovarian cancer patients was conducted at two US clinical trial sites: Johns Hopkins Hospital (Site JH) and M. D. Anderson Cancer Center (Site MDA).

4.1 Imprecision

As reported in the initial 510(k) submission (K964098) which was cleared on October 31, 1997, within-run and total assay imprecision were evaluated by testing five levels of Immuno 1 CA 125 II™ assay calibrators, BioRad Tumor Marker Controls, and an internal medical decision level serum pool (approximately 28 U/mL) over a period of twenty days of assay qualification runs. Imprecision was evaluated at three clinical trial sites: Site 1 was Bayer Corporation, Tarrytown, NY, Site 2 was Helsinki University Central Hospital, Finland and Site 3 was Hôpital Saint-Luc, Montreal Within-run imprecision ranged from 1.4% to 3.6% CV, and total imprecision ranged from 2.2% to 4.1% CV across products and sites. These results indicate that the recovery of Immuno 1 CA 125 II™ assay values are highly reproducible over time. Imprecision results are presented in Table 1.

Table 1: Immuno 1 CA 125 II™ Assay Imprecision

PRODUCT	MEAN	OBSERVATIONS	WITHIN-RUN		TOTAL	
			SD	CV	SD	CV
	(U/mL)	(n)	(U/mL)	(%)	(U/mL)	(%)
BioRad 1	24.7	667	0.90	3.6	1.02	4.1
MD Pool	26.1	677	0.61	2.3	0.87	3.3
BioRad 2	56.8	680	1.97	3.5	2.21	3.9
Cal 1	0.1	275	0.06	-	0.08	-
Cal 2	15.1	456	0.33	2.2	0.43	2.8
Cal 3	30.2	454	0.54	1.8	0.72	2.4
Cal 4	80.6	458	1.43	1.8	2.04	2.5
Cal 5	200.2	447	3.96	2.0	5.22	2.6
Cal 6	490.7	245	6.85	1.4	10.84	2.2

4.6 CLINICAL STUDIES

4.6.1 Introduction

To assess the safety and effectiveness of the Bayer Immuno 1™ CA 125 II Assay for monitoring ovarian cancer patients during the course of disease and therapy, clinical studies were performed at two investigational sites: Johns Hopkins Hospital (Site JH) and M. D. Anderson Cancer Center (Site MDA).

All patient samples were studied retrospectively. Assay values were determined for surplus serum samples which had been collected and stored (-70° C) in specimen banks prior to the study.

4.6.2 Serial Monitoring - Management Value of the Immuno 1 CA 125 II ™ Assay Results for Ovarian Cancer Patients

A retrospective clinical study was conducted to evaluate serial Immuno 1 CA 125 II Assay values in *78* ovarian cancer patients (Stages I - IV) during their course of disease and therapy. The study group included patients who responded to therapy, experienced disease progression, exhibited stable persistent disease, and demonstrated no clinical evidence of disease following treatment. *Of the 78 patients enrolled in the study, 5 patients were not evaluable due to the lack of hard clinical data to confirm their clinical status. These patients were placed in the "Indeterminate" column in Table 2 and were not used in the analysis.*

Table 2: Clinical Trial Results

Bayer Immuno 1 Longitudinal Patient Evaluation Results Ovarian Cancer Patients Only		
Correspondence (Parallels clinical course)	*N*	*Percentage*
Increasing CA 125 II with Progression	*24*	*33*
Decreasing CA 125 II with response	*19*	*26*
Increasing and decreasing CA 125 II with progression and response	*7*	*10*
Stable disease or No Evidence of Disease with no change in CA 125 II values	*8*	*11*
Total paralleling clinical course	*58*	*79*
No Correspondence (total) (Does not parallel the clinical course)	*15*	*21*

The correspondence of Immuno 1 CA 125 II™ assay levels with the clinical course of disease was evaluated similar to Bast *et al.*(16) by means of a doubling of CA 125 II values reflects disease progression and a 50% decrease in CA 125 II values reflects disease response to therapy. *Using these criteria, results shown in Table 3 demonstrate that the sensitivity of longitudinal measurements using the Bayer Immuno 1 CA 125 II™ assay as compared to the changes in clinical condition was 79%.*. The positive predictive value of an increase in assay values ≥ 100% into or within the abnormal (> 35 U/mL) range or a decrease in assay values ≥ 50% was *96%.*

Table 3: Evaluation Of Ovarian Cancer

		Clinical Status Change During The Profile Period		
	YES	NO	*Indeterminate*	TOTAL
CA 125 II Values: Increase ≥ 100% into or within the abnormal range (>35 U/mL) with clinical progression or decrease ≥ 50% with clinical response				
YES	*50*	*2*	*5*	*57*
NO	*13*	*8*		*21*
TOTAL	*63*	*10*	*5*	*78*

Sensitivity to change: *79% (58/73)*
Positive Predictive Value: *96% (50/52)*

These data support the clinical utility of the Immuno 1 CA 125 II™ Assay as an adjunctive test for use in the management (monitoring) of ovarian cancer patients during the course of disease and therapy.

4.6.3 Conclusions from the Clinical Studies

Results of the retrospective serial monitoring of patients with malignant ovarian disease confirm the safety and effectiveness of the Immuno 1 CA 125 II™ Assay as an aid in the management of ovarian cancer patients during the course of disease and therapy. This clinical study clearly demonstrates that the Immuno 1 CA 125 II™ Assay is sensitive to changes in disease status of ovarian cancer patients. The longitudinal trends of serum CA 125 II concentrations agreed well with clinical status in *58 of 78* patients studied with progression accompanied by a ≥ 100% increase in assay values into or within the abnormal range (> 35 U/mL), and response reflected by a ≥ 50% decrease in assay values. Longitudinal sensitivity to change in clinical condition was *79%*, and the positive predictive value of the test was *96 %*.

5. CONCLUSIONS DRAWN FROM ALL THE STUDIES

Valid Scientific Evidence

The conclusions drawn from these studies are based upon valid scientific evidence. Data were gathered following a well-designed protocol, in a research laboratory operating under the principles of Good Clinical Practices. Clinical data were gathered during well controlled investigations conducted by qualified experts. Patient case histories were well documented. The results of this study are comparable to literature reports of experiences with CA 125 assays (1-2, 5-7, 13-16).

Method Performance

Immuno 1 CA 125 II™ results are highly reproducible with a maximum inter-assay %CV pooled over reagent lots and clinical sites of 4.1% over the range of the assay. Other performance characteristics including analytical sensitivity and specificity, cross-reactivity, linearity, antigen excess hook effect, and parallelism were reported in the previous 510(k) for this assay (K964098) and meet the accepted specifications set for an assay of this type.

Safety and Effectiveness

These clinical studies confirm the safety and effectiveness of the Immuno 1 CA 125 II™ Assay as an aid in the management of ovarian cancer patients. The correlation between Immuno 1 CA 125 II™ concentrations and the patients' clinical course of disease demonstrate that the Immuno 1 CA 125 II™ Assay may be used in conjunction with other clinical indicators to confirm disease progression and response to therapy in ovarian cancer patients.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 14 1999

Mr. Gabriel J. Muraca, Jr.
Manager Regulatory Affairs
Bayer Corporation
511 Benedict Avenue
Tarrytown, New York 10591-5097

Re: K983715
Trade Name: Bayer Immuno 1™ CA 125 II™ Assay
Regulatory Class: II
Product Code: LTK
Dated: March 11, 1999
Received: March 15, 1999

Dear Mr. Muraca:

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 (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/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): K983715

Device Name: **Bayer Immuno 1™ CA 125II Assay**

Indications For Use:

The Bayer Immuno 1™ CA 125II Assay is an in vitro device for the quantitative measurement of OC 125 determinants associated with a high molecular weight glycoprotein in serum of women with epithelial invasive ovarian cancer. The Bayer Immuno 1™ CA 125II Assay is indicated as a one time test for use as an aid in the detection of residual or recurrent ovarian carcinoma in patients who have undergone first-line therapy and would be considered for second-look procedures. An assay value greater than 35 U/mL is predictive of residual disease provided alternative causes of an elevated CA 125II value can be excluded.

The Bayer Immuno 1™ CA 125II Assay is further indicated as an aid in the management (monitoring) of ovarian cancer patients when used in conjunction with other diagnostic procedures.

It is recommended that the Bayer Immuno 1™ CA 125II Assay be used under the order of a physician trained and experienced in management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer, or for use on any other system.

Peter E Maden

(Division Si
Division of
510(k) Num K983715

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)