K981397

SEP 18 1998

510 (k) Summary of Safety and Effectiveness

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

Name: **Address:**	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045
Telephone Number:	(213) 776-0180
Contact Person:	Edward M. Levine, Ph.D.
Date of Preparation:	September 15, 1998
Catalog Number:	LKOPZ, LKOP1, LKOP5 (50, 100, 500 tests)
Device Name **Trade:** **Common:**	IMMULITE® OM-MA Reagent system for the Determination of CA125 antigen in serum.
Classification:	LTK, Class II device
Manufacturer:	Euro/DPC Limited Glyn Rhonwy Llanberis, Gwynedd LL55 4EL United Kingdom (Manufactured under a Quality System-ISO 9002/EN29002/BS 5750)
Sole U. S. Importer:	Diagnostic Products Corporation (DPC) 5700 West 96th Street Los Angeles, CA 90045-5597
Establishment Registration #:	Euro/DPC – Not applicable DPC Registration number is 2017183
Substantially Equivalent: **Predicate Device:**	Centocor® CA 125 II™ RIA (P85009/S001- S007)

Description of Device:

IMMULITE® OM-MA is a clinical device for use with the IMMULITE Automated Immuno-assay Analyzer.

Intended Use of the Device:

IMMULITE® OM-MA is a clinical use device intended for use with the IMMULITE Automated Immunoassay Analyzer for the quantitative measurement of CA125 antigen in human serum. It is intended strictly for *in vitro* diagnostic use as an aid in monitoring the response to therapy for patients with epithelial ovarian cancer, and in detecting residual ovarian cancer in patients who have undergone first-line therapy and would be considered for diagnostic second-look procedures.

Summary and Explanation of the Test:

The CA125 determinant was originally identified by a monoclonal antibody, selected for reactivity with a cell line from a patient with serous papillary cystadenocarcinoma of the ovary. This antibody was found to react with cell lines derived from epithelial ovarian carcinomas but not with nonmalignant tissues including normal adult and fetal ovary.

Although the precise nature of the CA125 determinant remains unclear, there is agreement that the molecule is a high molecular weight (1000 kDa) glycoprotein with a smaller quantity of carbohydrate than mucins. There is some evidence that more than one form of the CA125 molecule exists.

Epithelial neoplasms of the ovary originate from the single layer of cells covering the ovary. These epithelial cells have a high proliferative capacity, repairing the ovarian surface after ovulation. Suppression of ovulation by oral contraceptives, pregnancy and lactation may therefore reduce the risk of ovarian cancer. Ovarian malignancy has been associated with a variety of peptide growth factors, oncogenes and tumor suppressor genes. According to a recent study comprising approximately 10% of the US population, more than 48% of ovarian cancer can be found in women 65 years of age and older, rather than in younger women. The incidence increases with age, reaching a peak of 54 in every 100,000 women in the age group 75 to 79 years.

Measurement of CA125 before and after cytoreductive surgery for ovarian cancer has been shown to predict the likelihood of a patient being left with residual disease.

IMMULITE OM-MA uses a murine monoclonal antibody for the capture and a rabbit polyclonal antibody for detection of the CA 125 antigen. The monoclonal antibody was established by immunization with human mucin prepared from a pool of patients with epithelial ovarian cancer. The monoclonal antibody, which forms the basis of specificity for the kit, recognizes a repetitive protein determinant expressed in the protein core of the CA 125 antigen. This antibody has specificity for an epitope that overlaps with, or is very near to, that bound by the M11 monoclonal antibody. The M11 monoclonal is incorporated in many commercially available CA 125 immunoassays. The polyclonal antibody is affinity purified against CA 125 antigen, resulting in a reagent reacting with multiple epitopes on this antigen.

Performance Equivalence - Technology Comparison:

IMMULITE® OM-MA is a solid-phase, chemiluminescent immunometric assay. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with a murine monoclonal antibody specific for CA 125. The patient sample and alkaline phosphatase - conjugated rabbit polyclonal anti-CA 125 antibody (Reagent A) are incubated for approximately 60 minutes in the Test Unit, with intermittent agitation. Reagent B, consisting of a buffer with preservative, is added after the first 30-minute cycle. CA 125 in the sample is bound to form an antibody sandwich complex. Unbound enzyme conjugate is then removed by a centrifugal wash, after which substrate is added and the Test Unit is incubated for a further 10 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, 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, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is proportional to the concentration of CA 125 in the sample.

The Centocor® CA 125 II™ RIA is a one-step "sandwich" radioimmunoassay. Polystyrene beads coated with the M11 capture antibody reactive with molecules containing OC 125 reactive determinants are incubated with the patient sample, standards or control, and tracer. The tracer, composed of ^{125}I labeled (mouse monoclonal) OC 125 quantifies the number of OC 125 reactive determinants and is distinct from the solid phase antibody. During this incubation, molecules which contain OC 125 reactive determinants form "sandwich" complexes with the monoclonal antibodies. Unbound materials present in the patient sample are removed by aspiration of the fluid and washing of the beads. The bound radioactivity is determined by counting the beads in a gamma counter. The bound radioactivity is proportional to the concentration of the OC 125 reactive determinant (antigen) in the patient sample within the working range of the assay. A standard curve is obtained by plotting the U/mL of CA 125 II Standards vs. bound radioactivity (CPMs). The CA 125 assay values for patient samples and controls, run concurrently with the standards, can be determined from the standard curve.

Performance Equivalence - Method Comparison:

The clinical performance of the IMMULITE OM-MA procedure was evaluated in two clinical sites in the United States. Thirty serially monitored ovarian cancer patients each provided between 4 and 41 serial specimens over the course of their disease, during which the patients manifested several clinical incidents (regression, stability and progression). IMMULITE OM-MA measurements of CA 125 were examined and compared with the clinical status. The association between clinical status and the IMMULITE OM-MA CA-125 measurements is presented below.

	IMMULITE OM-MA Test Results			
Clinical Status	CA 125 Increasing	CA 125 Stable	CA 125 Decreasing	Total
Regression	0	2	15	17
Stable	11	21	4	36
Progression	12	6	0	18
Total	23	29	19	71

$\chi^2 = 50.7$, $df = 4$, $p < 0.00001$

The IMMULITE OM-MA procedure was also compared to Centocor CA 125 II, a commercially available RIA, on 165 samples from healthy male and female individuals (ranging from 17 to 80 years of age), and also from patients with ovarian carcinoma and other malignant diseases (ranging from 26 to 81 years of age), with CA 125 concentrations ranging from 1.4 to 411 U/mL, as measured by the IMMULITE OM-MA assay. Linear regression analysis yielded the following statistics:

(IML) = 0.77 (Centocor) – 3.7 U/mL $r = 0.974$

Mean: 35.2 U/mL (IMMULITE OM-MA)
50.7 U/mL (Centocor CA 125 II)

95% Confidence Intervals:
0.7 to 0.8 for slope
-6.3 to -1.1 for intercept

Conclusion:

The conclusions drawn from the clinical and nonclinical studies demonstrate that the device is safe, effective, and performs as well as, or better than, the current legally marketed device.

Edward M. Levine, Ph.D.
Director of Clinical Affairs

9/15/98
Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 18 1998

Edward M. Levine, Ph.D.
Director of Clinical Affairs
Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, CA 90045

Re: K981297
Trade Name: IMMULITE® OM-MA
Regulatory Class: II
Product Code: LTK
Dated: June 22, 1998
Received: June 23, 1998

Dear Dr. Levine:

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 requirement, 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.

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): K981297

Device Name: **IMMULITE® OM-MA**

Indications For Use:

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Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K981297

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

(Optional Format 1-2-96)