K972021

510 (k) Summary
Safety and Effectiveness

OCT 31 1997

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:	May 30, 1997
Device Name: **Trade:** **Catalog Number:** **Common:**	 IMMULITE® Third Generation PSA LKUP1 (100 tests); LKUP5 (500 tests) Reagent system for the determination of prostate specific antigen in human serum.
Classification:	Class II device, 82LTJ
Manufacturer:	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045
Establishment Registration #:	DPC's Registration # is 2017183
Substantially Equivalent Predicate Device:	Hybritech Tandem-R® PSA TOSOH AIA-PACK® PA
Description of Device:	IMMULITE Third Generation PSA is a clinical device for use with the IMMULITE Automated Immunoassay Analyzer.
Intended Use of the Device:	IMMULITE Third Generation PSA is designed for the quantitative detection of prostate specific antigen in human serum. It is intended strictly for *in vitro* diagnostic use as an aid in the management of cancer patients.

Summary and Explanation of the Test:

Prostate specific antigen (PSA), first identified and characterized by Wang et al in 1979, is a glycoprotein monomer with protease activity. PSA has an isoelectric point of approximately 6.9 and a molecular weight of approximately 33-34 kilodaltons, containing approximately 10% carbohydrate by weight. Subsequently, the amino acid sequence of PSA was reported and the gene has been cloned. PSA is biochemically and immunologically distinct from PAP and does not exhibit enzymatic phosphatase activity.

PSA is localized in the cytoplasm of prostatic ductal epithelium and in secretions of the ductal lumina. Because PSA is a secretory protein of the prostate, it can be recovered and purified both from prostatic tissue and from seminal plasma. PSA has been found to be extensively associated with prostate tissue; and elevated serum PSA has been found in patients with prostate cancer, benign prostatic hypertrophy or hyperplasia (BPH), and inflammatory conditions of other adjacent genitourinary tissues, but not in healthy men, men with nonprostatic carcinoma, healthy women or women with cancer.

Serum PSA is not recommended as a guide in disease staging. The combination of PSA measurement and rectal examination with ultrasonography, in the event of abnormal findings, may provide a better method of detecting prostate cancer than rectal examination alone.

PSA determinations can be useful in detecting metastatic or persistent disease in patients following surgical or medical treatment of prostate cancer. Persistent elevation of PSA following treatment or an increase in the pretreatment PSA concentration is indicative of recurrent or residual disease. Hence, PSA is widely accepted as an aid in the management of prostate cancer patients.

Summary and Explanation of the Device:

DPC's IMMULITE Third Generation PSA assay is an in vitro diagnostic for use with DPC's IMMULITE Automated Immunoassay Analyzer, a random access instrument. The IMMULITE Automated Immunoassay Analyzer has been previously cleared for marketing by DPC's wholly-owned subsidiary, Cirrus Diagnostics Inc. (K905215). The assay is intended for the quantitative measurement of PSA in human serum as an aid in the management of prostate cancer patients. The IMMULITE Third Generation PSA assay is a solid-phase, two-site sequential chemiluminescent immunometric assay. The solid phase consists of a polystyrene bead (coated with a monoclonal antibody specific for PSA) which is enclosed within an IMMULITE Test Unit (LUP1) which acts as a reaction vessel. The patient serum sample (or PSA Adjustors, LUPL and LUPH) and a reagent (LUPA, a protein buffer/serum matrix, with preservative) are simultaneously introduced and incubated for approximately 30 minutes at 37°C in the Test Unit. With intermittent agitation, PSA in the sample becomes bound to the surface of the bead. Unbound serum is then removed by a centrifugal wash. A second reagent (LUPB, alkaline phosphatase-conjugated polyclonal antibody) is introduced, and the Test Unit is incubated for another 30-minute cycle. Unbound enzyme conjugate is removed by a centrifugal wash, after which a chemiluminescent substrate (LSUB, a phosphate ester of adamantyl dioxetane) is added and the Test Unit is incubated for a further 10 minutes. The substrate 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 thus also the photon output as measured by the luminometer) is proportional to the concentration of PSA in the sample. The concentration of PSA in the patient sample is obtained using a stored master calibration curve within the IMMULITE analyzer. The IMMULITE Third Generation PSA assay has a calibration range up to 20 nanograms of PSA per milliliter.

Performance Equivalence - Technology Comparison:

Diagnostic Products Corporation (DPC) asserts that IMMULITE® Third Generation PSA is substantially equivalent to the Hybritech Tandem-R® PSA kit marketed by Hybritech, Inc. San Diego, CA and the Tosoh AIA-PACK® PA marketed by Tosoh Medics, Inc, Foster City, CA.

Each product is designed for the quantitative measurement of prostate specific antigen (PSA) in serum. Each product is intended as an aid in the management of prostate cancer patients.

IMMULITE® Third Generation PSA is a chemiluminescent enzyme immunoassay, Hybritech Tandem-R PSA is an immunoradiometric assay, and the Tosoh AIA-PACK PA is an immunoenzymometric assay. The technology in DPC's IMMULITE® Third Generation PSA is identical to technology used in previously cleared and commercially marketed IMMULITE® products.

In the Hybritech assay, the patient sample is reacted with a plastic bead coated with a monoclonal antibody directed toward a unique site on the PSA molecule and, simultaneously, with a radiolabeled monoclonal antibody directed against a distinctly different antigenic site on the same PSA molecule. Following the formation of the solid phase/PSA/labeled antibody sandwich, the bead is washed to remove unbound labeled antibody. The radioactivity bound to the solid phase is measured in a gamma counter. The amount of radioactivity measured is directly proportional to the concentration of PSA present in the test sample, which is determined from a standard curve.

In the Tosoh assay, PSA is bound with monoclonal antibody immobilized on a magnetic solid phase. The magnetic beads are washed to remove unbound enzyme-labeled monoclonal antibody and are then incubated with a fluorogenic substrate. The amount of enzyme-labeled monoclonal antibody that binds to the beads is directly proportional to the PSA concentration in the test sample.

Performance Equivalence - Method Comparison:

In an outside study, the clinical performance of the IMMULITE® Third Generation PSA was compared to both the Hybritech Tandem-R® and Tosoh AIA-PACK® PA. Linear regression analysis of 285 specimens, with PSA concentrations ranging from approximately 0.3 to 20 ng/mL, that were assayed by both the IMMULITE and Hybritech assays yielded:

$$\text{IMMULITE}^{®} = 0.85 * \text{Hybritech} + 0.16 \text{ ng/mL}$$

with a correlation coefficient (r) of 0.964.

Linear regression analysis of the 162 specimens, with PSA concentrations ranging from 0.1 to 13 ng/mL, that were assayed by both the IMMULITE and Tosoh assays yielded:

$$\text{IMMULITE}^{®} = 0.93 * \text{Tosoh} - 0.04 \text{ ng/mL}$$

with a correlation coefficient (r) of 0.989.

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

5/21/97

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

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 31 1997

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

Re: K972021
Trade Name: IMMULITE® Third Generation PSA LKUP1 (100 tests); LKUP5 (500 tests)
Regulatory Class: II
Product Code: LTJ
Dated: September 15, 1997
Received: September 17, 1996

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.

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: **IMMULITE Third Generation PSA**

Indications For Use:

DPC's IMMULITE Third Generation PSA is intended for use with the IMMULITE Automated Immunoassay Analyzer. The IMMULITE Third Generation PSA is a solid-phase, chemiluminescent enzyme immunoassay designed for the quantitative measurement of prostate specific antigen (PSA) in serum. It is intended as an adjunctive test to aid in the management of prostate cancer.

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Peter E Maloney

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K978021

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

(Optional Format 1-2-96)