

K980833

MAY 1 1998

**510 (k) Summary
Safety and Effectiveness**

This summary of safety and effectiveness information has been prepared in accordance with the requirements of SMDA 1990 and 21 CFR Part 807.92.

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

Telephone Number: (213) 776-0180
Facsimile Number: (213) 776-0204

Contact Person: Edward M. Levine, Ph.D.
Director of Clinical Affairs

Date of Preparation: April 21, 1998

Device Name: IMMULITE[®] Pylilinks[®]-D
Trade: Reagent system for the determination of deoxypyridinoline in urine.

Catalog Number: LKPD1 (100 tests), LKPD5 (500 tests)

Classification: Class I device, 75-JMM
CLIA Complexity Category: Moderate, based on previous classification of analogous tests.

Manufacturer: Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045-5597

Establishment Registration Number: DPC's Registration Number is 2017183

Substantially Equivalent Predicate Device: Metra Biosystems[®] Pylilinks[®]-D (K974260)

Description of Device: IMMULITE[®] Pylilinks[®]-D is a clinical device for use with the IMMULITE[®] Automated Immunoassay Analyzer.

Intended Use of the Device: The IMMULITE[®] Pylilinks[®]-D assay is designed for the quantitative measurement of deoxypyridinoline in urine. It is intended strictly for *in vitro* diagnostic use in monitoring type 1 collagen resorption changes, especially in bone in post menopausal women diagnosed with osteoporosis and receiving antiresorptive therapy (amino-bisphosphonate).

Summary and Explanation of the test:

Approximately 90% of the organic matrix of bone is type I collagen, a triple helical protein. Type I collagen of bone is crosslinked by specific molecules which provide rigidity and strength. Crosslinks of mature type I collagen in bone are the pyridinium crosslinks, pyridinoline (PYD) and deoxypyridinoline (DPD). DPD is formed by the enzymatic action of lysyl oxidase on the amino acid lysine. DPD is released into the circulation during the bone resorption process. DPD is excreted unmetabolized in urine and is unaffected by diet, making it suitable for assessing resorption.

Bone is constantly undergoing a metabolic process called remodeling. This includes a degradation process, bone resorption, mediated by the action of osteoblasts. Remodeling is required for the maintenance and overall health of bone and is tightly coupled; that is, resorption and formation are in balance. In abnormal states of bone metabolism, this process becomes uncoupled and, when resorption exceeds formation, this results in a net loss of bone. The measurement of specific degradation products of bone matrix provide analytical data of the rate of bone metabolism.

Osteoporosis is a metabolic bone disease characterized by abnormal bone remodeling. It is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in susceptibility to fractures. The most common type of osteoporosis occurs in postmenopausal women as a result of the estrogen deficiency produced by the cessation of ovarian function. Restoration of premenopausal estrogen levels by replacement therapy prevents bone loss and osteoporosis. Estrogens and a class of compounds known as bisphosphonates are antiresorptive therapies which can be used to prevent bone loss or treat osteoporosis. Osteoporosis can also result from attaining an inadequate peak bone mass during the growing years, an age-related imbalance of bone remodeling with a net excess of resorption, and a number of clinical conditions and therapies which induce bone loss or bone remodeling imbalances. These include endocrine diseases such as hypogonadism, hyperthyroidism, hyperparathyroidism, and hypercortisolism; gastrointestinal diseases related to nutrition and mineral metabolism; connective tissue diseases; multiple myeloma; chronic immobilization, alcoholism, or tobacco use; and chronic therapy with heparin or corticosteroids. Other diseases characterized by abnormal bone remodeling include Paget's disease and cancers metastatic to bone.

A clinical study was successfully conducted to establish the safety and efficacy of the Ppyrilinks-D assay to monitor changes in urinary DPD excretion associated with amino-bisphosphonate (alendronate) antiresorptive therapy. The results from this study indicate that the Ppyrilinks-D assay is safe and effective for monitoring the antiresorptive effect of amino-bisphosphonate (alendronate) therapy among subjects diagnosed with osteoporosis.

Technological Comparison to Predicate:

Diagnostic Products Corporation (DPC) asserts that DPC's IMMULITE[®] Pyrilinks[®]-D is substantially equivalent to Metra Biosystems[®] Pyrilinks[®]-D. Both products are intended for *in vitro* diagnostic use.

IMMULITE[®] Pyrilinks[®]-D is a solid-phase, chemiluminescent immunoassay for use with the IMMULITE Automated Immunoassay Analyzer. The solid-phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with a monoclonal antibody specific for DPD.

The patient sample and alkaline phosphatase-conjugated DPD are simultaneously introduced into the Test Unit, and incubated for approximately 30 minutes at 37° C with intermittent agitation. During this time, DPD in the sample competes with enzyme-labeled DPD for a limited number of antibody-binding sites on the bead. Unbound material 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 inversely proportional to the concentration of DPD in the sample.

The Metra Biosystems[®] Pyrilinks[®]-D procedure is a competitive enzyme immunoassay in a microtiter stripwell format utilizing a monoclonal anti-DPD antibody coated on the strip to capture DPD. 50 µL of diluted standards, controls, and samples are added to each microtiter well of the anti-DPD coated strips. 100 µL of cold enzyme conjugate is then added to each well, the wells are covered and incubated in the dark for 2 hours at 2-8 °C. Each well is then washed three times with wash buffer and 150 µL of working substrate solution is added to each well. After the wells are incubated for 60 minutes at room temperature, 100 µL of stop solution is added and the optical density is read at 405 nm. the concentration of DPD in the sample is determined from the standard curve using quantitation software with a 4-parameter calibration curve fitting equation.

Performance Equivalence:

Diagnostic Products Corporation asserts that the IMMULITE[®] Pyrilinks[®]-D produces substantially equivalent results to other commercially marketed deoxypyridinoline assays, such as Metra Biosystems[®] Pyrilinks[®]-D. Each product is intended strictly for *in vitro* diagnostic use in monitoring type 1 collagen changes, especially in bone in postmenopausal women diagnosed with osteoporosis and receiving antiresorptive therapy (amino-bisphosphonate).

Method Comparison:

The IMMULITE[®] Pylilinks[®]-D procedure was compared to the Metra Biosystems[®] Pylilinks[®]-D on seventy-five (75) patient urine samples, with DPD concentrations ranging from approximately 7.6 to 280 nM.

Mean Values: 70 nM (IMMULITE[®] Pylilinks[®]-D)
 70 nM (Metra Biosystems[®] Pylilinks[®]-D)

Linear regression analysis of IMMULITE[®] Pylilinks[®]-D values yielded the following statistics:

$$(\text{IMMULITE}^{\text{®}} \text{ Pylilinks}^{\text{®}}\text{-D}) = 1.00 (\text{Metra Biosystems}^{\text{®}} \text{ Pylilinks}^{\text{®}}\text{-D}) + 0.57 \text{ nM} \quad r = 0.966$$

Conclusion:

The data presented in this summary of safety and effectiveness is the data that the Food and Drug Administration used in granting DPC substantial equivalence for IMMULITE[®] Pylilinks[®]-D.

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

Date



MAY 1 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Edward M. Levine, Ph.D.
Director of Clinical Affairs
Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045-5597

Re: K980833
IMMULITE® Pyrilinks®-D
Regulatory Class: I
Product Code: JMM
Dated: March 2, 1998
Received: March 4, 1998

Dear Dr. Levin:

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 (Pre-market 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 pre-market 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.

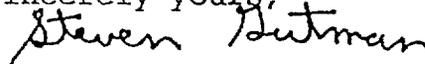
Page 2

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/dsmamain.html>".

Sincerely yours,



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): K980833_____

Device Name: IMMULITE[®] Pylinks-D

Indications For Use:

IMMULITE Pylinks-D is a solid-phase, chemiluminescent enzyme immunoassay for use with the IMMULITE Automated Analyzer and is designed for the quantitative measurement of deoxypyridinoline (DPD) in urine. It is intended strictly for *in vitro* diagnostic use in monitoring type 1 collagen resorption changes, especially in bone in post menopausal women diagnosed with osteoporosis and receiving antiresorptive therapy (amino-bisphosphonate).

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

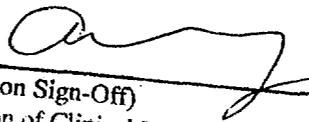
Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓
(Per 21 CFR 801.109)

OR

Over-The-Counter Use _____

(Optional Format 1-2-96)



(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K 980833