K993254

NOV 12 1999

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:	Diagnostic Products Corporation
Address:	5700 West 96th Street Los Angeles, California 90045-5597
Telephone Number: **Facsimile Number:**	(310) 645-8200 (310) 645-9999
Contact Person:	Edward M. Levine, Ph.D. Director of Clinical Affairs
Date of Preparation:	October 26, 1999
Device Name:	IMMULITE® 2000 Folic Acid
Trade:	Reagent system for the determination of folic acid in serum, heparinized plasma, or whole blood.
Catalog Number:	L2KFO2 (200 tests); L2KFO6 (600 tests)
Classification:	Class II device (862.1295, 75CGN)
Manufacturer:	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045-5597
Establishment Registration #:	DPC's Registration # is 2017183
Substantially Equivalent Predicate Device:	DPC's IMMULITE® Folic Acid (K943705)
Description of Device:	IMMULITE® 2000 Folic Acid is a clinical device for use with the IMMULITE® 2000 Automated Immunoassay Analyzer.

Intended Use of the Device:

IMMULITE® 2000 Folic Acid is for *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of folic acid in serum, heparinized plasma or ascorbic acid-treated whole blood, as an aid in clinical diagnosis and treatment of anemia.

Summary and Explanation of the Test:

Folic acid (folate) and vitamin B12 are nutrients essential to hematopoiesis. Megaloblastic anemia is almost always due to lack of one of these two vitamins. Circulating folate levels are usually normal or elevated in vitamin B12 deficiency, but red cell folate levels are frequently low in this condition.

Folate deficiency is commonly encountered as a result of dietary deficiency (as in alcoholism) or increased demand for this vitamin (as in pregnancy). Unlike vitamin B12, folate is a heat-labile vitamin susceptible to loss by prolonged cooking. Accordingly, the prevalence of folate deficiency exhibits major demographic variations, apparently reflecting differences in dietary and culinary habits.

Circulating folate levels, being strongly influenced by recent intake, are unreliable as an index to tissue stores. Thus, folate levels measured in serum or plasma may be normal in the face of folate deficiency. Conversely, circulating levels may be low long before tissue stores have been exhausted. Accordingly, it is important to measure red cell folate levels whenever serum or plasma levels are measured.

Performance Equivalence - Technology Comparison:

IMMULITE® and IMMULITE® 2000 Folic Acid are chemiluminescent immunoassays. The technology in DPC's IMMULITE® 2000 Folic Acid is a unique combination of technologies employed in previously cleared and commercially marketed DPC products.

The **IMMULITE 2000 Folic Acid** assay begins with a 2-cycle, on-board sample treatment of patient serum, plasma or ascorbic acid-treated whole blood (for measuring red cell folate). The sample, along with ligand-labeled folic acid, is first treated with dithiothreitol (DTT), in a reaction tube containing no bead, and then with sodium hydroxide/potassium cyanide (NaOH/KCN), in a second treatment cycle. The treated sample is transferred to a second reaction tube containing a murine anti-folate binding protein antibody-coated polystyrene bead and folate binding protein (FBP). During a 30-minute incubation, folic acid released from binding proteins in the patient sample competes with ligand-labeled folic acid for binding with FBP. The bead is washed and alkaline phosphatase labeled anti-ligand is added. During the final 30-minute incubation, the alkaline phosphatase anti-ligand binds to the ligand-labeled folate that was bound to the bead during the first incubation. The unbound enzyme conjugate is removed by centrifugal wash. Substrate is then added.

Technology Comparison (continued):

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, is then added and the test unit is incubated for a further 10 minutes. The chemiluminescent substrate undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. Production of this intermediate results in a sustained emission of light. The bound complex – and thus also the photon output – is inversely proportional to the concentration of folic acid in the sample.

IMMULITE® Folic Acid is a boil, competitive, liquid-phase, ligand-labeled, protein binding chemiluminescent assay with *in situ* immobilization, and with an anti-ligand detection system. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with a murine monoclonal antibody specific for folic acid binding protein. The sample is pretreated by boiling in the presence of dithiothreitol to denature endogenous binding proteins to release folic acid. The treated patient sample, ligand-labeled folic acid analog and folic acid binding protein are simultaneously introduced into the Test Unit, and incubated for approximately 30 minutes at 37 °C with intermittent agitation. During this time, folic acid in the sample competes with the ligand-labeled folic acid analog for a limited amount of folic acid binding protein, and the folic acid binding protein is captured by the antibody on the bead. Unbound analog is then removed by a centrifugal wash, after which an alkaline phosphatase-anti-ligand conjugate is introduced and the test unit is incubated for an additional 30 minute cycle. The unbound enzyme conjugate is removed by a centrifugal wash.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, is then added and the test unit is incubated for a further 10 minutes. The chemiluminescent substrate undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. Production of this intermediate results in a sustained emission of light. The bound complex – and thus also the photon output – is inversely proportional to the concentration of folic acid in the sample.

Method Comparison:

Serum

The IMMULITE® 2000 Folic Acid procedure was compared to DPC's IMMULITE® Folic Acid on 156 serum samples, with folic acid concentrations ranging from 1.8 to 20 ng/mL.

Means: 8.3 ng/mL (IMMULITE® 2000)
9.2 ng/mL (IMMULITE®)

Linear regression analysis of folic acid values yielded the following statistics:

(IMMULITE® 2000) = 0.96 (IMMULITE®) - 0.54 ng/mL r = 0.996

Hemolysates

The IMMULITE® 2000 Folic Acid procedure was also compared to DPC's IMMULITE® Folic Acid on 49 samples, with folic acid concentrations ranging from 46 to 260 ng/mL.

Means: 128 ng/mL (IMMULITE® 2000 Folic Acid)
134 ng/mL (IMMULITE® Folic Acid)

Linear regression analysis of folic acid values yielded the following statistics:

(IMMULITE® 2000) = 1.18 (IMMULITE®) - 29 ng/mL r = 0.981

Conclusion:

The data presented in this summary of safety and effectiveness is the data the Food and Drug Administration used in granting DPC substantial equivalence for IMMULITE® 2000 Folic Acid.

Edward M. Levine

10/26/99

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

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 1 2 1999

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

Re: K993254
Trade Name: Immulite® 2000 Folic Acid
Regulatory Class: II
Product Code: CGN
Dated: September 24, 1999
Received: September 28, 1999

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 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):_____

Device Name: **IMMULITE® 2000 Folic Acid**

Indications For Use:

IMMULITE 2000 Folic Acid is for *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of folic acid in serum, heparinized plasma or ascorbic acid-treated whole blood, as an aid in clinical diagnosis and treatment of anemia.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K993254

(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)