K993251

NOV 17 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:	September 24, 1999
Device Name:	IMMULITE® 2000 Vitamin B12
Trade:	Reagent system for the determination of vitamin B12 in serum and heparinized plasma
Catalog Number:	L2KVB2 (200 tests); L2KVB6 (600 tests)
Classification:	Class II device, 75-CDD (21CFR 862.1810)
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® Vitamin B12
Description of Device:	IMMULITE® 2000 Vitamin B12 is a clinical device for use with the IMMULITE® 2000 Automated Immunoassay Analyzer.

Intended Use of the Device:

IMMULITE® 2000 Vitamin B12 is for *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of vitamin B12 in serum or heparinized plasma, as an aid in clinical diagnosis and treatment of anemia.

Summary and Explanation of the Test:

Vitamin B12 (cobalamin) and folate are nutrients essential to hematopoiesis. Megaloblastic anemia is almost always due to lack of one of these two vitamins. Vitamin B12 deficiency can also result in severe neurological impairment.

Circulating levels of vitamin B12 are usually a good index to tissue stores. That is, vitamin B12 levels as measured in serum or plasma by an optimized assay system are typically low in vitamin B12 deficiency, and normal or elevated otherwise. Exceptions to this rule can occur in those relatively uncommon situations where levels of vitamin B12 transport proteins are abnormal. Thus, low circulating vitamin B12 levels can occur in the absence of vitamin B12 deficiency where the level of transcobalamin I (a physiologically inactive transport protein) is low.

Conversely, vitamin B12 deficiency can occur in the presence of normal or even elevated plasma vitamin B12 levels where transcobalamin II levels are low or where levels of inactive vitamin B12 transport proteins are high, as in chronic myelogenous leukemia. (Circulating folate levels are usually normal or elevated in vitamin B12 deficiency, but red cell folate levels are frequently low in this condition.)

Vitamin B12 deficiency occurs only rarely as a result of dietary lack of this vitamin. More commonly, it results from impaired absorption, as in partial or total gastrectomy, or in pernicious anemia, a condition characterized by absence or near absence of intrinsic factor. Since roughly two thirds of all patients with pernicious anemia have blocking antibodies to intrinsic factor (IFbAb), while IFbAb are only very rarely encountered in other situations, IFbAb determinations represent a useful follow-up test for the differential diagnosis of vitamin B12 deficiency. (Circulating intrinsic factor antibodies are present in more than half of all pernicious anemia patients. Increased transport protein levels can occur, for example in chronic myelogenous leukemia.)

Common causes of high vitamin B12 levels include liver disease, myeloproliferative disease (with chronic myelogenous leukemia as a special case) and the use of multivitamin supplements.

Performance Equivalence - Technology Comparison:

IMMULITE® and IMMULITE® 2000 Vitamin B12 are chemiluminescent immunoassays. The technology in DPC's IMMULITE® 2000 Vitamin B12 is a unique combination of technologies employed in previously cleared and commercially marketed DPC products.

The **IMMULITE 2000 Vitamin B12** assay begins with a one-cycle sample treatment of patient serum or plasma with dithiothreitol (DTT) and a sodium hydroxide/potassium cyanide solution (NaOH/KCN) in a reaction tube containing no bead. After a 30-minute incubation, the treated sample is transferred to a second reaction tube containing a vitamin B12-coated polystyrene bead, hog intrinsic factor (HIF) and an alkaline phosphatase-labeled antibody specific for HIF. During a 30-minute incubation, the vitamin B12 released from endogenous binding proteins during sample treatment competes with immobilized vitamin B12 for binding with HIF. Alkaline phosphatase-labeled anti-HIF antibody binds to HIF and is immobilized only if HIF is bound to the B12-coated bead. Unbound enzyme conjugate is removed by centrifugal wash. Substrate is added.

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 vitamin B12 in the sample.

IMMULITE® Vitamin B12 is a chemiluminescent version of the classic method for vitamin B12 radioassay, involving a preliminary heat denaturation step. Vitamin B12 in the patient sample is released from carrier proteins by incubation at 100 °C in the presence of dithiothreitol and potassium cyanide to inactivate vitamin B12-binding proteins, even at extreme levels, as well as antibodies to intrinsic factor.

After the heat denaturation step, the treated patient sample and purified hog intrinsic factor are simultaneously introduced into an IMMULITE® Test Unit containing a polystyrene bead coated with a B12 analog, and incubated for approximately 30 minutes at 37 °C with intermittent agitation. During this incubation, vitamin B12 in the treated sample competes with the B12 analog on the solid phase for a limited number of vitamin B12 binding sites on the purified intrinsic factor. (Endogenous vitamin B12 analogs do not interfere, because the binder is free of R-protein.) Alkaline phosphatase-labeled anti-hog intrinsic factor is introduced, and the Test Unit is incubated for another 30-minute cycle. The unbound enzyme conjugate is removed by a centrifugal wash.

Performance Equivalence - Technology Comparison (continued):

Substrate is then 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 vitamin B12 in the sample.

Performance Equivalence - Method Comparison:

The IMMULITE® 2000 Vitamin B12 procedure was compared to DPC's IMMULITE® Vitamin B12 on 166 patient serum samples. Linear regression yielded the following results.

(IMMULITE® 2000) = 0.95 (IMMULITE®) - 34 pg/mL r = 0.937

Means: 400 pg/mL (IMMULITE® 2000)
457 pg/mL (IMMULITE®)

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 Vitamin B12.

Edward M. Levine

9/24/99

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 17 1999

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

Re: K993251
Trade Name: IMMULITE® 2000 Vitamin B12
Regulatory Class: II
Product Code: LIG
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): K993251

Device Name: **IMMULITE® 2000 Vitamin B12**

Indications For Use:

IMMULITE 2000 Vitamin B12 is for *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of vitamin B12 in serum or heparinized plasma, as an aid in clinical diagnosis and treatment of anemia.

Dyan Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K993251

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Concurrence of CDRH, Office of Device Evaluation (ODE)

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

(Optional Format 1-2-96)