3/12/99

K982466

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: **Address:**	Diagnostic Products Corporation 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:	February 12, 1999
Device Name:	
Trade:	IMMULITE Thyroglobulin
Catalog Number:	LKTYZ (50 tests), LKTY1 (100 tests), LKTY5 (500 tests)
Common:	Reagent system for the determination of thyroglobulin in serum or heparinized plasma.
Classification:	Class II device, 82-JZO (21CFR 866.5870)
Manufacturer:	EURO/DPC Ltd. (Manufacturing under a Quality System – ISO9001/EN29001/BS 5750
Sole U.S. Importer:	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045-5597
Establishment Registration Number	EURO/DPC: Not applicable DPC: 2017183
Substantially Equivalent Predicate Device:	ORGenTec Thyroglobulin ELISA (K972190) Manufactured by ORGenTec, and distributed in the USA by ALPCO, Windham, NH
Description of Device:	IMMULITE Thyroglobulin is a clinical device for use with the IMMULITE Automated Immunoassay Analyzer.

Intended Use of the Device:

IMMULITE Thyroglobulin is a two-site chemiluminescent enzyme immunometric assay for use with the IMMULITE Analyzer and designed for the quantitative measurement of thyroglobulin in serum or heparinized plasma. It is intended strictly for *in vitro* diagnostic use as an aid in monitoring patients who have undergone thyroidectomy.

Performance Equivalence:

Diagnostic Products Corporation (DPC) asserts that the IMMULITE Thyroglobulin produces substantially equivalent results to other commercially marketed thyroglobulin assays, such as the ORGenTec Thyroglobulin ELISA. Each product is intended strictly for *in vitro* diagnostic use to aid in the clinical diagnosis of thyroid diseases.

Summary and Explanation of the Test:

Thyroglobulin (TG) is a heterogeneous iodoglycoprotein which has a molecular mass of approximately 660,000 daltons. Thyroglobulin is normally synthesized in the follicular cells of the thyroid gland, under the influence of thyrotropin, and represents the precursor to thyroxine and the other iodothyronines.

The expected upper limit of normal for circulating thyroglobulin is approximately 40 to 60 ng/mL, with a median of 5 to 10 ng/mL. Somewhat higher values are encountered in newborns and during the third trimester of pregnancy. Thyroglobulin levels also tend to be elevated in regions of endemic goiter.

The major clinical applications for measurement of this prohormone derive from the fact that functioning thyroid tissue, whether normal or neoplastic, appears to be the only source of circulating thyroglobulin. Accordingly, thyroglobulin determinations have been widely used to complement radioiodine scanning and other techniques (such as ultrasound or immunohistochemical staining) as an aid in identifying the presence or absence of functioning thyroid tissue, or an increase in such tissue relative to an individually established baseline. The differential diagnosis of congenital hypothyroidism and the management of nonmedullary differentiated thyroid carcinoma constitute two well-established contexts of use for this application of serum thyroglobulin measurements.

Congenital Hypothyroidism

Thyroglobulin determinations have been used, sometimes in conjunction with ultrasound and radioiodine scanning, to help clarify the type of thyroid defect in previously diagnosed congenital hypothyroidism. Very low or undetectable thyroglobulin levels are expected in infants born without thyroid tissue (thyroid agenesis), whereas higher, but widely varying levels are generally encountered in infants with hypoplastic thyroid glands, ectopic thyroid tissue, dyshormonogenic goiter, congenital TBG deficiency or transient hypothyroidism.

Summary and Explanation of the Test (continued):

Other Applications

Thyroglobulin measurements may also be of value in helping to distinguish subacute thyroiditis from thyrotoxicosis caused by covert administration of thyroid hormones. In the latter event, low levels of thyroglobulin are expected due to thyroid hormone suppression of thyrotropin.

Technological Comparison to Predicate:

IMMULITE Thyroglobulin is a chemiluminescent enzyme-labeled immunometric assay, based on ligand-labeled monoclonal antibody and separation by anti-ligand-coated solid phase.

The patient sample, a ligand-labeled anti-thyroglobulin monoclonal antibody and an alkaline phosphatase-labeled anti-thyroglobulin polyclonal antibody are simultaneously introduced into the Test Unit containing immobilized anti-ligand, and incubated for approximately 60 minutes at 37°C with intermittent agitation. During this time, thyroglobulin in the sample forms an antibody sandwich complex which, in turn, binds to anti-ligand on the solid phase. Unbound conjugate is removed by a centrifugal wash; 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 proportional to the concentration of thyroglobulin in the sample.

The **ORGenTec Thyroglobulin** assay is an indirect solid phase enzyme immunometric assay based on precoated microplates in strip format (12x8 wells), ideal for smaller runs, or economical batch processing. The Thyroglobulin assay takes place in three separate phases:

Phase 1:
Microplate wells are coated with highly specific anti-TG antibodies. Standards, controls and undiluted patient samples are pipetted into the wells of the first microplate. Sample buffer is added to appropriate wells. Recovery control is added to patient sample for recovery test. Any thyroglobulin molecules present bind to the inner well surfaces. After a 60 minute incubation, the microplate is washed with wash buffer to remove non-reactive serum components.

Phase 2:
An anti-thyroglobulin peroxidase conjugate solution is pipetted into the microplate wells which recognizes the thyroglobulin bound to the immobilized antibody. After a 60 minute incubation, excess conjugate is washed away.

Technological Comparison to Predicate (continued):

Phase 3:
A chromogenic substrate solution containing TMB (3,3',5,5'-tetramethyl-benzidine) is pipetted into the microplate wells. During a 15 minute incubation, the solution changes to a blue color. 1 M hydrochloric acid is added to stop color development.

The amount of color is directly proportional to the concentration of TG present in the original sample. The optical density for each standard may be graphically plotted against the concentration of TG and unknowns extrapolated from the curve. Optical density is read at 450 nm. Bichromatic measurement with a 650 nm reference is recommended.

Method Comparison:

The IMMULITE Thyroglobulin procedure was compared to Kit A (ALPCO's ORGenTec), a commercially available indirect solid phase enzyme immunometric assay for thyroglobulin, on 150 samples from patients with Hashimoto's disease, Graves disease, patients who had undergone thyroidectomy, as well as euthyroid individuals. The thyroglobulin concentrations of these specimens covered the entire calibration range of the assay. The data were tabulated in reference to the respective assays' suggested cutoffs, with the following results:

		IMMULITE	
Kit A	>50	10	0
	<=50	9	131
		>55	<=55

N	150
Agreement	94.0%
Sensitivity	100.0%
Specificity	93.6%

95% Confidence Limits for Relative Sensitivity and Specificity, respectively: 69.2% - 100%, 88.2% - 97%.

The same data, excluding one specimen in the above analysis due to its thyroglobulin level exceeding both assays' upper calibration limits, yielded the following result in a linear regression analysis:

IMMULITE = 2.16 × Kit A + 0.76 ng/mL r = 0.95

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 Thyroglobulin.

Edward M. Levine

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

2/12/98

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR 12 1999

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

Re: K982466
Trade Name: IMMULITE® Thyroglobulin Model LKTY
Regulatory Class: II
Product Code: MSW
Dated: February 12, 1999
Received: February 16, 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 at (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):_____

Device Name: **IMMULITE® Thyroglobulin**

Indications For Use:

IMMULITE Thyroglobulin is a two-site chemiluminescent enzyme immunometric assay for use with the IMMULITE Analyzer and designed for the quantitative measurement of thyroglobulin in serum or heparinized plasma. It is intended strictly for *in vitro* diagnostic use as an aid in monitoring patients who have undergone thyroidectomy.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K982466

(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)