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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:** December 11, 1997

**Device Name**  
**Trade:** IMMULITE® Free T3  
**Common:** Reagent system for the determination of free T3 in serum

**Catalog Number:** LKF31 (100 tests), LKF35 (500 tests)

**Classification:** Class II device, 75-CDP (21 CFR 862.1710)  
**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:** Chiron Diagnostics' ACS:180 Free T3 (K932747)

**Description of Device:** IMMULITE® Free T3 is a solid-phase, Chemiluminescent enzyme immunoassay for use with the IMMULITE® Automated Immunoassay Analyzer.

**Intended Use of the Device:** The IMMULITE® Free T3 assay is designed for the quantitative measurement of non-protein-bound triiodothyronine (free T3) levels in serum. It is intended strictly for *in vitro* use as an aid in the clinical assessment of thyroid status.

### **Summary and Explanation of the Test:**

Under normal physiological conditions triiodothyronine (T3) represents approximately 5 percent of the thyroid hormone in plasma. Although present in lower concentration than thyroxine (T4), T3 has greater metabolic activity, faster turnover and a larger volume of distribution. It is produced largely through extrathyroidal conversion of T4. Like T4, it circulates almost entirely bound to the carrier proteins TBG, pre-albumin and albumin. Free T3 constitutes only about 0.25% of the total T3 in circulation.

Measurement of total T3 by immunoassay has a number of well-established uses. In the presence of elevated free or total T4, total T3 measurements help confirm a hyperthyroidism diagnosis. Abnormal elevation of total T3 may also occur when the total T4 concentration is normal - a condition known as "T3 toxicosis."

For the most part, free T3 levels correlate closely with total T3 levels. Total T3, however, depends not only on thyroid status and the peripheral conversion of T4 to T3, but also on the concentration of thyroid hormone-binding proteins. Free T3, on the other hand, is largely unaffected by variations in these carrier proteins. Thus, the TBG elevations typical of pregnancy, oral contraceptive use, and estrogen therapy effects an increase in the total T3 level while leaving the free T3 concentration basically unchanged.

The free T3 concentration typically reflects a patient's actual thyroid status more reliably than the total T3 concentration.

### **Technological Comparison to Predicate:**

IMMULITE Free T3 is a solid-phase, competitive, analog, sequential chemiluminescent immunoassay. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with a monoclonal antibody specific for T3.

The patient sample and ligand-labeled T3 analog are simultaneously introduced into the Test Unit, and incubated for approximately 30 minutes at 37°C with intermittent agitation. During this time, free T3 in the sample competes with the ligand-labeled T3 analog for a limited number of antibody binding sites on the bead. Unbound analog is then removed by a centrifugal wash.

An alkaline phosphatase-labeled anti-ligand is introduced, and the Test Unit is incubated for approximately another 30-minute cycle. The unbound enzyme 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 inversely proportional to the concentration of free T3 in the sample.

The IMMULITE Free T3 procedure is a direct or single test assay, in the sense that its results are not calculated as a function of total T3, but interpolated from a (stored) standard curve calibrated in terms of free T3 concentrations. In this respect it differs from classic equilibrium dialysis methods and from so-called free T3 index determinations as well. It requires neither a pre-incubation step nor preliminary isolation of the free fraction by dialysis or column chromatography.

The IMMULITE Free T3 system has been optimized to eliminate all binding of the ligand-labeled T3 analog to endogenous proteins, while leaving essentially undisturbed the original equilibrium between free and protein-bound T3 in the patient sample. The analog itself has no measurable affinity for thyroxine-binding globulin (TBG), the principal thyroid hormone transport protein. To prevent binding of the ligand-labeled T3 analog to albumin, blocking agents are present, at a concentration carefully adjusted to avoid displacement of native T3 from endogenous carrier proteins. To further minimize the risk of "stripping," the system employs an antibody, at low concentration, with an affinity for T3 slightly less than that of albumin, and operates under physiological conditions of temperature, pH and ionic strength.

The ACS:180 Free T3 assay is a competitive immunoassay using direct, chemiluminescent technology. FT3 in the sample competes with a T3 analog, which is covalently coupled to paramagnetic particles in the Solid Phase for a limited amount of acridinium ester-labeled monoclonal mouse anti-T3 antibody in the Lite Reagent.

An inverse relationship exists between the amount of FT3 present in the patient sample and the amount of relative light units (RLUs) detected by the system.

### **Method Comparison:**

The IMMULITE® Free T3 (2-Step) procedure was compared to Chiron Diagnostics' ACS:180 Free T3 assay on 237 patient samples, with free T3 concentrations ranging from approximately 1.3 to 19 pg/mL. Linear regression analysis yielded the following statistics:

$$(\text{IMMULITE}^{\circledR} \text{ Free T3 2-Step}) = 0.99 (\text{ACS:180 Free T3}) - 0.11 \text{ pg/mL} \quad r = 0.930$$

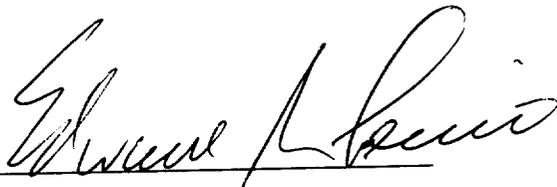
Mean Values:            3.13 pg/mL (IMMULITE® Free T3 2-Step)  
                                 3.28 pg/mL (ACS:180 Free T3)

### **Performance Equivalence:**

Diagnostic Products Corporation asserts that IMMULITE® Free T3 is substantially equivalent to other commercially marketed free T3 assays, such as ACS:180 Free T3. Each product is intended strictly for *in vitro* diagnostic use as an aid in the clinical assessment of thyroid status.

**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® Free T3.



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



**Date**



Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

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• Director of Clinical Affairs  
Diagnostic Products Corporation  
5700 West 96th Street  
Los Angeles, California 90045-5597

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Re: K974634  
IMMULITE Free T3  
Regulatory Class: II  
Product Code: CDP  
Dated: December 11, 1997  
Received: December 12, 1997

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 (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 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.

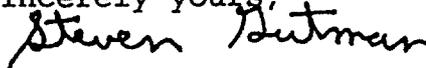
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

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

