

K983972

DEC 7 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 96<sup>th</sup> Street  
Los Angeles, California 90045-5597

**Telephone Number:** (310) 645-8200  
**Facsimile Number:** (310) 645-9999

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

**Date of Preparation:** November 30, 1998

**Device Name:**  
**Trade:** IMMULITE<sup>®</sup> Troponin I

**Catalog Number:** LKTI1 (100 tests), LKTI5 (500 tests)

**Common:** Reagent system for the determination of troponin I in serum, heparinized or EDTA plasma.

**Classification:** Class II device, 75-MMI (21CFR 862.1215)

**Manufacturer:** Diagnostic Products Corporation  
5700 West 96<sup>th</sup> Street  
Los Angeles, California 90045-5597

**Sole U.S. Importer:** Diagnostic Products Corporation  
5700 West 96<sup>th</sup> Street  
Los Angeles, California 90045-5597

**Establishment Registration Number** DPC's Registration Number is 2017183

**Substantially Equivalent Predicate Device:** Stratus<sup>®</sup> Cardiac Troponin-I Fluorometric Enzyme Immunoassay (K951890)

**Description of Device:** IMMULITE<sup>®</sup> Troponin I is a clinical device for use with the IMMULITE<sup>®</sup> Automated Immunoassay Analyzer.

### **Intended Use of the Device:**

IMMULITE<sup>®</sup> Troponin I is a solid-phase, two-site chemiluminescent enzyme immunometric assay for use with the IMMULITE Automated Analyzer and designed for the quantitative measurement of troponin I in serum, heparinized or EDTA plasma. It is intended for *in vitro* use as an aid in the diagnosis of acute myocardial infarction (AMI).

### **Performance Equivalence:**

Diagnostic Products Corporation (DPC) asserts that the IMMULITE<sup>®</sup> Troponin I assay produces substantially equivalent results to other commercially marketed troponin I assays, such as the Stratus<sup>®</sup> Cardiac Troponin-I. Each product is intended strictly for *in vitro* diagnostic use to aid in the clinical diagnosis of acute myocardial infarction.

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

Acute myocardial infarction (AMI) is usually diagnosed on the basis of chest pain, electrocardiographic changes, and elevations of markers of myocardial injury. The MB isoenzyme of creatine kinase (CK-MB) has been the preferred marker for two decades. A study by Wu, et al found excellent clinical sensitivity of the CK-MB assay between 6 and 24 hours following onset of AMI, with decreased sensitivity beginning in the 24 to 48-hour interval. However, CK-MB levels can also increase in patients with acute or chronic muscle disease who lack apparent cardiac injury. In the same study, myoglobin, a muscle protein considered to be an early marker of AMI, became elevated within 6 hours of onset, achieved peak clinical sensitivity in the interval 6 to 12 hours following onset, and no longer offered diagnostic value by hour 24. Myoglobin, although valuable for the early information it provides, also lacks specificity for cardiac injury. A marker specific for myocardial injury is therefore highly desirable.

Cummins, et al reported the release of cardiac troponin I (cTnI) in AMI. Many studies have focused on cTnI as a candidate marker with acceptable sensitivity and specificity for AMI and other cardiac diseases.

Troponin, a molecule that binds to the thin filament (actin) of striated muscle fibers, acts with intracellular calcium to control the interaction of the thin filament with the thick filament (myosin), thus regulating muscle contraction. Troponin consists of three subunits: T, which connects the troponin complex and tropomyosin (another cardiac muscle regulatory protein); I, which prevents muscle contraction in the absence of calcium; and C, which binds calcium. Cardiac troponin I (MW 22.5 kDa) and the two skeletal muscle isoforms of troponin I have considerable amino acid sequence homology, but cTnI contains an additional N-terminal sequence and is highly specific for myocardium.

### **Summary and Explanation of the Test (continued):**

Clinical studies report several desirable features of cTnI as a marker of myocardial injury. cTnI rises early in AMI patients and attains levels that are clearly separated from baseline values, so that by 7 hours following onset, the cTnI test detects 95 percent of patients in whom AMI will be

confirmed. Plasma values of cTnI remain elevated for several days, providing a long window for detection of cardiac injury. cTnI has also demonstrated value for predicting mortality risk in unstable angina and in non-Q wave myocardial infarction.

cTnI has demonstrated equivalent diagnostic accuracy for AMI when compared with lactate dehydrogenase type 1 and CK-MB, and may clarify diagnosis in contexts where elevated CK-MB cannot be attributed with certainty to cardiac injury alone. These include surgery, traumatic injury, renal failure, seizures, and skeletal muscle myopathies.

In addition, a study on patients undergoing coronary artery bypass grafting (CABG) showed cTnI to be a sensitive marker for perioperative myocardial infarction (PMI); the peak concentration and time of peak both served as diagnostic criteria.

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

**IMMULITE<sup>®</sup> Troponin I** is a solid-phase, two-site chemiluminescent immunometric assay. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with a monoclonal antibody specific for troponin I. While the patient sample and alkaline phosphatase-conjugated polyclonal antibody are incubated for 30 minutes at 37 °C in the Test Unit with intermittent agitation, troponin I in the sample is bound to form an antibody sandwich complex. Unbound conjugate 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 proportional to the concentration of troponin I in the sample.

The **Stratus Cardiac Troponin-I** assay is an automated, two-site immunoassay which utilizes two monoclonal antibodies that are specific for the cardiac isotype of troponin-I. In this procedure, the sample is pipetted onto the center portion of a square piece of glass fiber filter paper which contains the monoclonal antibody responsible for capture of the analyte. After a short incubation, a conjugate reagent, containing a monoclonal antibody labeled with alkaline phosphatase, is pipetted onto the reaction zone. During the second incubation period, the labeled antibody reacts with the cardiac troponin-I which has been bound by the capture antibody. Any unbound labeled antibody is subsequently eluted from the reaction zone of the

**Technological Comparison to Predicate (continued):**

solid support by applying a substrate wash solution to the center of the reaction zone. By including substrate for alkaline phosphatase in the wash solution, initiation of enzyme activity occurs simultaneously with radial partitioning of the bound and unbound fractions of the labeled antibody. The enzymatic rate generated by the bound antibody fraction, which is directly proportional to the concentration of troponin-I in the sample, is measured by front surface fluorescence. The rate generated by the specimen is compared to a stored standard curve by the microprocessor portion of the analyzer, which then calculates the concentration of analyte in the sample.

To perform measurements of cardiac troponin-I, tabs (solid phase), conjugate reagent, assay diluent, and specimens are placed in their designated positions on the Stratus analyzer. Once the assay run has been programmed, all subsequent steps are performed by the analyzer. Time from initiation of an assay to first result is 10 minutes.

**Method Comparison:**

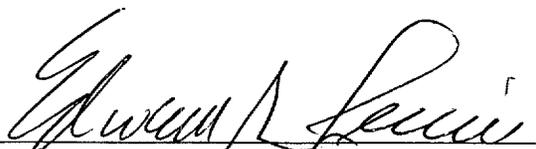
The IMMULITE Troponin I procedure was compared to a commercially available immunofluorescent assay for Troponin I (Stratus Cardiac Troponin-I) on 97 serum samples with Troponin I concentrations ranging from nondetectable to approximately 180 ng/mL. Linear regression analysis yielded the following statistics:

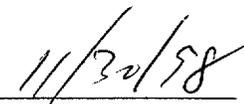
$$\text{IMMULITE} = 1.00 \times (\text{Kit A}) - 0.25 \text{ ng/mL } r = 0.91$$

Means: 15.6 (IMMULITE)  
15.8 (Kit A)

**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® Troponin I.

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

  
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Date



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

DEC 7 1998

Edward M. Levine, Ph.D.  
Director, Clinical Affairs  
DIAGNOSTIC PRODUCTS CORPORATION  
5700 West 96<sup>th</sup> Street  
Los Angeles, CA 90045

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Re: K983972

Trade Name: IMMULITE® Troponin I  
Regulatory Class: II  
Product Code: MMI  
Dated: November 6, 1998  
Received: November 9, 1998

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.

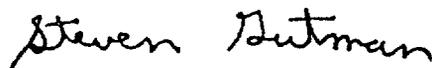
If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially 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.

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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 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): K983972

Device Name: IMMULITE® Troponin I

Indications For Use:

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Concurrence of CDRH, Office of Device Evaluation (ODE)

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Prescription Use  
(Per 21 CFR 801.109)

OR

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Over-The-Counter Use

(Optional Format 1-2-

96)

[Signature]  
(Division Sign-Off)  
Division of Clinical Laboratory Devices  
510(k) Number K983972