

JUN 10 1998

K981495

**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.

Device Name:

Trade: IMMULITE® CK-MB

Catalog Number: LKCP1 (100 tests), LKCP5 (500 tests)

CFR: Device intended to measure the activity of the enzyme creatine phosphokinase isoenzymes (a group of enzymes with similar biological activity) in plasma and serum. Measurements of creatine phosphokinase isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

Common: Reagent system for the determination of creatine kinase isoenzyme MB in heparinized plasma or serum.

Classification: Class II device, 75-JHX (21 862.1215)

Panel: Clinical Chemistry

CLIA Complexity

Category: We believe the category to be moderate, based on previous classification of analogous tests.

Manufacturer: Diagnostic Products Corporation (DPC)
5700 West 96th Street
Los Angeles, CA 90045-5597

**Establishment
Registration #:**

DPC's establishment Registration No. is 2017183

**Substantially Equivalent
Predicate Device:**

Roche® Isomune® -CK (K903025)

Description of Device:

IMMULITE® CK-MB is a two-site chemiluminescent enzyme immunometric assay for use with the IMMULITE® Automated Analyzer.

**Intended Use of the
Device:**

IMMULITE® CK-MB is a two-site chemiluminescent enzyme immunometric assay for use with the IMMULITE® Automated Analyzer and designed for the quantitative measurement of creatine kinase isoenzyme MB (CK-MB) antigen in heparinized plasma or serum. It is intended strictly for *in vitro* use as an aid in patient management and the assessment of prognosis of myocardial infarction.

Summary and Explanation of the test:

Creatine kinase (CK) is an enzyme, found primarily in muscle and brain tissue, which exists as three dimeric isoenzymes – CK-MM (CK-3), CK-MB (CK-2), and CK-BB (CK-1) – built from subunits designated M and B. The CK-MB isoenzyme, which has a molecular mass of approximately 87,000 daltons, accounts for 5 to 50% of total CK activity in myocardium. In skeletal muscle, by contrast, it normally accounts for just 1% or less, CK-MM being the dominant form, though the percentage can be as high as 10% in conditions reflecting skeletal muscle injury and regeneration (e.g. severe exercise, muscular dystrophy, polymyositis).

CK-MB is one of the most important myocardial markers (in spite of not being altogether cardiac-specific), with well-established roles in confirming acute myocardial infarction (AMI) and in monitoring reperfusion during thrombolytic therapy following AMI.

In AMI, plasma CK-MB typically rises some 4 to 6 hours after the onset of chest pains, peaks within 12 to 24 hours, and returns to baseline levels within 24 to 48 hours. The pattern of serial CK-MB determinations is more informative than a single determination: one CK-MB measurement, even when taken at an appropriate time, cannot definitively confirm or rule out the occurrence of AMI. High levels might reflect skeletal injury rather than myocardial damage. A value within the reference range might be significant if it represents an increase from the patient's baseline level. (Low baseline levels are sometimes encountered in the elderly.) Accordingly, it has been recommended that CK-MB be measured on admission to the emergency room, and at intervals thereafter: for example, at 3-hour intervals over a 6 to 9-hour period in patients with nonspecific electrocardiogram changes; or at 6 to 8-hour intervals over a 24-hour period and more frequently if thrombolytic therapy has been instituted.

Thrombolytic therapy, if successful, leads to an "enzyme washout" evidenced by a sharp increase in circulating CK-MB levels as early as 90 minutes after the initiation of therapy. Accordingly, serial CK-MB levels have been used in this context to assess reperfusion.

Technological Comparison to Predicate:

Provided for the reviewer is a comparison of DPC's IMMULITE[®] CK-MB System vs. Roche[®] Isomune[®] -CK technology. This section does not contain any new information for a reviewer who is familiar with the DPC IMMULITE[®] System based upon the review of previous IMMULITE[®] assay submissions.

IMMULITE[®] CK-MB 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-CK-MB monoclonal antibody and an alkaline phosphatase-labeled anti-CK-BB polyclonal antibody are simultaneously introduced into the Test Unit containing immobilized anti-ligand, and incubated for approximately 30 minutes at 37°C with intermittent agitation. During this time, CK-MB 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.

Technological Comparison to Predicate (continued):

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 CK-MB in the sample.

In the **Roche® Isomune® -CK**, the specific measurement of CK-MB in serum in the presence of other CK isoenzymes is based on the method originally reported by Wicks et al. Patient serum is placed in two tubes and goat anti-serum to CK-MM is added to the first tube. This tube is allowed to incubate for 10 minutes to completely inhibit all M-subunit activity. To the second tube is added anti-CK-MM bound to donkey anti-goat gammaglobulin on an inert polymer particle and after a 5 minute incubation the tube is centrifuged to remove the insoluble particles containing bound M subunit isoenzymes. Quantitative measurement of residual CK enzyme activity in both tubes is performed with an appropriate CK substrate reagent.

The enzymatic activity in the first tube will reflect the contribution from the CK-B subunits present as components of both CK-MB and CK-BB isoenzymes, plus any contribution from adenylate kinase. The enzymatic activity of the second or blank tube will reflect the activity of the CK-BB isoenzyme, macro CKs and adenylate kinase. By subtracting the activity of the second or blank tube from the activity in the first tube, the enzymatic activity due to the B subunit of CK-MB will be obtained. CK-MB activity is then obtained by multiplying this value by two.

Performance Equivalence:

Diagnostic Products Corporation asserts that the IMMULITE® CK-MB produces substantially equivalent results to other commercially marketed creatine kinase isoenzyme MB assays, such as Roche® Isomune® -CK. Each product is designed for the quantitative measurement of CK-MB in heparinized plasma or serum. Each product is intended strictly for *in vitro* diagnostic use as an aid in the patient management and the assessment of prognosis of myocardial infarction.

Method Comparison:

The IMMULITE[®] CK-MB procedure was compared to the Roche[®] Isomune[®] -CK on forty-three (43) patient samples, with CK-MB concentrations ranging from approximately 16 to 177 ng/mL.

Mean Values: 42 ng/mL (IMMULITE[®] CK-MB)
 51 ng/mL (Roche[®] Isomune[®] -CK)

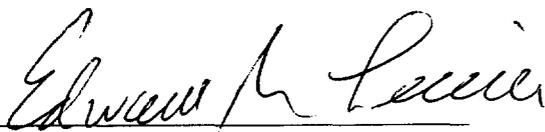
Linear regression analysis of IMMULITE[®] CK-MB values yielded the following statistics:

$$\text{(IMMULITE[®] CK-MB)} = 0.84 \text{ (Roche[®] Isomune[®] -CK)} - 1.36 \text{ ng/mL}$$

$r = 0.912$

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[®] CK-MB.





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

Date



JUN 10 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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

Re: K981495
IMMULITE® CK-MB
Regulatory Class: II
Product Code: JHS, JIT, JJX
Dated: April 24, 1998
Received: April 27, 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 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 pre-market 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.

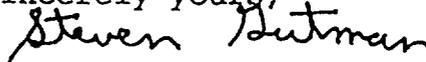
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

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

