

Summary of 510(k) Safety and Effectiveness

NOV 10 1997

1. General Information

Device Generic Name: Enzyme Immunoassay, Troponin I
Device Trade Name: ACCESS® Troponin I assay
Applicant's Name and Address: Sanofi Diagnostics Pasteur, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318

2. Predicate Device

Baxter Stratus® Cardiac Troponin-I Fluorometric Enzyme Immunoassay
Baxter Diagnostics, Inc.
Deerfield, IL 60015-4633

3. Device Description

The ACCESS® Troponin I assay is a paramagnetic-particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I levels in human serum and plasma (EDTA), using the ACCESS® Immunoassay System.

4. Comparison of Technological Characteristics

The ACCESS® Troponin I test and the Stratus® Cardiac Troponin-I test are for the measurement of cardiac Troponin I in human serum. Both tests utilize the binding of cardiac Troponin I to specific monoclonal antibodies in a two site "sandwich" immunoassay. Both tests utilize alkaline phosphatase enzyme conjugated to monoclonal antibody. The ACCESS® Troponin I test uses a dioxetane-based chemiluminescent substrate, while the Stratus® Cardiac Troponin I test uses 4-Methylumbelliferyl Phosphate as the substrate. The ACCESS® Troponin I test measures light production from a chemiluminescent reaction while the Stratus® Cardiac Troponin I test measures front surface fluorescence. The ACCESS® Troponin I test uses lyophilized calibrators prepared from buffered human serum matrix with human cardiac troponin I at specified levels, while the Stratus® Cardiac Troponin I test uses liquid calibrators (shipped frozen on dry ice) prepared from buffered bovine protein matrix and human cardiac troponin I at specified levels.

5. Summary of Analytical Studies

Precision study: Total imprecision ranges from 5.97% CV (high human serum based control) to 13.53% CV (low human serum based control).
Dilution Recovery: Linearity studies performed by diluting four human serum samples containing Troponin I with Troponin I Diluent gives an average recovery of 93.5%.
Correlation: A comparison of serum Troponin I values from 189 samples run in both the ACCESS® Troponin I assay and the Stratus® Cardiac Troponin I test gives the following statistical data: $r = 0.87$, $y = 0.136x - 0.088$.
Analytical Sensitivity: The lowest detectable level of troponin I distinguishable from zero (Troponin Calibrator S0) with 95% confidence is 0.03 ng/ml.

6. Summary of Clinical Performance

The purpose of this multi-site prospective study was to 1) establish the clinical performance characteristics of the ACCESS® Troponin I assay, and 2) demonstrate substantially equivalent performance to a previously cleared troponin I assay and to the current gold standard biochemical marker, CK-MB.

For this study, 289 subjects presenting to the emergency department with chest pain of 20 minutes duration were followed serially to rule-in or rule-out AMI. Each patient contributed a minimum of two serum samples to establish the diagnosis. Forty five (45) subjects ruled-in for AMIs.

Summary of 510(k) Safety and Effectiveness (con't)

ROC curve analysis of all subject results demonstrated an optimal cutoff of 0.15 ng/ml for this clinical indication. Using 0.15 ng/ml as a decision level, the ACCESS® Troponin I assay demonstrated a clinical sensitivity of 89% and a clinical specificity of 91%. Results from 201 patients in which both the ACCESS® Troponin I and the Stratus® Troponin I assays were used, demonstrate 90% concordance. ACCESS® Troponin I assay results were 90% concordant with CK-MB results in 208 subjects tested with both devices.

The sensitivity and specificity of the ACCESS® Troponin I assay was similar to both CK-MB and Stratus® Troponin I when analyzed as a function of time. All assays showed peak sensitivity at 5-11 hours after the onset of chest pain. Both troponin I assays demonstrated peak specificity at 12-23 hours after the onset of chest pain.

ACCESS® Troponin I demonstrated a high degree of specificity in subjects with skeletal muscle injuries and renal disease, two clinical groups that can confound the diagnosis of AMI. The specificity of ACCESS® Troponin I in 58 skeletal injury patients was 86%, which is similar to that of Stratus® Troponin I. For renal disease patients, the specificity of ACCESS® Troponin I assay was 96% for 81 subjects tested.

In conclusion the data demonstrate acceptable diagnostic efficiency of the ACCESS® Troponin I assay reagents when utilized with the ACCESS® Immunoassay Analyzer.

7. Conclusion

The ACCESS® Troponin I reagents when utilized with the ACCESS® Immunoassay Analyzer are substantially equivalent to another test currently in commercial distribution for the measurement of cardiac Troponin I.



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 10 1997

• Jan Olsen
Supervisor, Regulatory Affairs
Beckman Instruments, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318

Re: K974075
Trade Name: ACCESS[®] Troponin I
Regulatory Class: II
Product Code: MMI
Dated: October 28, 1997
Received: October 29, 1997

Dear Ms. Olsen:

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 (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 requirement, 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 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): K974075

Device Name: ACCESS® Troponin I

Indications For Use:

The ACCESS® Troponin I assay is a paramagnetic-particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I levels in human serum and plasma (EDTA), using the ACCESS® Immunoassay System.

Summary and Explanation:

Cardiac troponin I (cTnI, molecular weight : 22,500 Da) is a contractile protein exclusively present in the cardiac muscle (1,2). Troponin I is one of three subunits of the troponin complex (I, T, C), which with tropomyosin are bound to actin in the thin filament of the myofibril. Its physiological role is to inhibit the ATPase activity of the actin-myosin complex in the absence of calcium, and therefore, to prevent muscular contraction (3).

Three tissue isoforms have been identified:

- fast troponin I and slow troponin I with molecular weights of 19,800 Da each, expressed in fast twitch and slow twitch skeletal muscle fibers, respectively.
- cardiac troponin I with a N-terminal site having an additional chain of 30 amino acid residues.

Cardiac Troponin I levels in acute myocardial infarction (AMI) exhibit similar rise and fall patterns to those found in CK-MB. Cumulative data from several studies indicate Troponin I levels are detectable (above quoted values for non-AMI samples) 3-6 hours after the onset of chest pain. Troponin I levels peak at approximately 12-16 hours and can remain elevated for 4-9 days post AMI. These same studies noted that the time to peak concentration of cTnI occurred later in patients who did not receive thrombolytic therapy (4,5,6).

Sequencing of cardiac troponin I from mammals has shown important differences between the cardiac (7) and skeletal (8) forms. Skeletal muscle does not express cardiac troponin I, either during development or in response to stimuli (9). No cross reactivity with skeletal troponin I isoforms allows distinction between cardiac and skeletal injuries, and allows diagnosis of myocardial infarction associated with muscle lesions (rhabdomyolysis, polytraumatism) (6,9,10,11).

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Patricia Bernhardt (for M. Montgomery)

(Division Sign-Off)

Division of Clinical Laboratory Devices

510(k) Number K974075

Prescription Use (Per 21 CFR 801.109)

OR

Over-The Counter Use