IV. 510(K) SUMMARY: CARESIDE™ CKMB SAFETY AND EFFECTIVENESS

I. Applicant Information

A.	Applicant Name	**CARESIDE, Inc.**
B.	Applicant/Manufacturer Address	6100 Bristol Parkway Culver City, CA 90230
C.	Telephone Number	310-338-6767
D.	Contact Person	Kenneth B. Asarch, Pharm.D., Ph.D.
E.	FAX Number	310-338-6789
F.	e-Mail Address	AsarchK@CARESIDE.com
G.	Date 510(k) Summary prepared	January 29, 1999

II. Device Information

A.	Device Name (Trade)	**CARESIDE™ CKMB**
B.	Device Name (Classification)	CK-MB test system
C.	Device Classification	Clinical chemistry panel CK-MB test system Regulation Number: 21 CFR 862.1215 Regulatory Class II Classification Number: to be assigned
D.	Special controls and performance standards	None applicable

III. Substantial Equivalence Claim

A. General equivalency claim

The ability to monitor analyte-specific biochemical reactions in dry film and other formats is widely recognized and has gained widespread acceptance for use in chemistry assays.

CK-MB *in vitro* diagnostic products, in both dry film and other formats, are already on the U.S. market, including CK-MB products which are based upon immunoinhibition.

B. Specific equivalency claim

This CARESIDE™ CKMB test is substantially equivalent in principle, intended use, and clinical performance to the currently marketed Vitros slides for the quantitative measurement of CK-MB on the Vitros DTSC module of the Vitros DT II system.

Name of Predicate Device:	Johnson and Johnson's (formerly Eastman Kodak, Inc.) **Vitros CKMB Slides** for Johnson and Johnson's **Vitros DTSC module of the Vitros DT II system** (formerly Eastman Kodak's DTSC 60 II).
Predicate Device 510K number:	**K912844/A**
Product Code:	unknown

IV. Device Description

CARESIDE™ CKMB cartridges are used with the CARESIDE, Inc. CARESIDE *Analyzer*™ to measure CK-MB activity in whole blood, serum or plasma specimens. The CARESIDE™ CKMB cartridge, a single use disposable *in vitro* diagnostic test cartridge, delivers a measured volume of serum or plasma to a dry film to initiate the measurement of CK-MB activity. The film cartridge (patent pending) contains all reagents necessary to measure CK-MB activity.

A. Explanation of Device Function

Each CARESIDE™ CKMB cartridge consists of a CK-MB-specific multi-layer reagent film mounted in a plastic base with a hinged lid. The user introduces the specimen into the cartridge Sample Well, closes the lid and inserts the cartridge into the CARESIDE *Analyzer*™.

Once loaded, the CARESIDE *Analyzer*™ scans the cartridge barcode, brings the cartridge and the contained specimen to 37°C, and spins the cartridge to move the sample from the Sample Well into the cartridge channels and chambers. 8.5 µL of sample remains in the metering passage. Any excess sample flows into an overflow well.

The sample is automatically dispensed onto the multi-layer reagent film. The spreading layer distributes the specimen uniformly. In this layer CK-M activity is inhibited by the anti-CK-M subunit antibody contained in the layer. The CK-B subunit is not inhibited by the antibody but rather is activated by N-acetylcysteine. The CK-B activity is stoichometrically related to the CK-MB activty. The CK-B catalyzes the reaction of creatine phosphate with ADP, producing creatine and ATP. ATP reacts with endogenous glucose in a hexokinase-catalyzed reaction to produce glucose-6-phosphate and ADP. G-6-P is then oxidized by glucose-6-phosphate dehydrogenase producing nicotinamide adenine dinucleotide (NADH). NADH reduces nitrotetrazolium blue in a diaphorase catalyzed reaction, producing a diformazan dye. The rate of change of the color intensity of the resulting reddish dye, as measured by the amount of reflected light at 570 nanometers, directly relates to the specimen CK-MB activity.

Test Reaction Sequence:

$$\text{CK-MM, CK-MB} \xrightarrow{\text{Anti-CK-M antibody}} \text{CK-B}$$

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow[\text{NAC, } Mg^{+2}]{\text{CK-B}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{Glucose} \xrightarrow[Mg^{+2}]{\text{Hexokinase}} \text{ADP} + \text{G-6-P}$$

$$\text{G-6-P} + NAD^{+} \xrightarrow{\text{G6PDH}} \text{6-phosphogluconic acid} + \text{NADH} + H^{+}$$

$$\text{NTB} + \text{NADH} \xrightarrow{\text{Diaphorase}} \text{Diformazan dye} + NAD^{+}$$

As the cartridges spin, a photodiode measures reflectance of light emitted by a wavelength-specific light emitting diode (LED) over a fixed time period. The analyzer uses the reflectance measurements and the lot-specific standard curve to calculate CK-MB activity.

B. Test Summary

Creatine kinase (CK) is an enzyme consisting of two sub-units (termed B and M) that catalyzes the reversible phosphorylation of creatine by adenosine-triphosphate (ATP) to creatine phosphate and adenosine-diphosphate (ADP). Only the CK dimer has enzymatic activity. Thus, active CK occurs as CKBB, CKMB and CKMM isoenzymes. These are also referred to as CK-1, CK-2 and CK-3 respectively, according to their differential mobility on an electrophoretic gel.

Each CK isoenzyme is found in a particular tissue. CKBB (CK-1) is found in the brain, prostate, gut, lung, bladder, uterus, placenta and thyroid. CKMB (CK-2) is found in the heart muscle and CKMM (CK-3) is found in skeletal and cardiac muscle. Thus, the measurement of CK and its various isoenzymes is important in the diagnosis of several diseases, especially in myocardial infarction.

In myocardial infarction, the first 4 to 6 hours are characterized by a rise in the total CK activity, reaching a peak value between 18 and 30 hours and returning to normal by the third day. This rise is followed by a rise of the CKMB (CK-2) fraction, which reaches a maximum about 12-14 hours after a myocardial infarction. It should be noted that CKMB (CK-2) breaks down faster then CKMM (CK-3), and so may return to normal levels 48-72 hours post-infarction. CKMB levels are used as an indication and measure of myocardial damage. Other cardiac conditions such as angina pectoralis, cardiogenic shock, electrical countershock, tachycardia, myocarditits and congestive heart failure have been reported as having a low occurrence of elevated total CK and CKMB (CK-2). Cardiac trauma resulting from heart surgery will cause an elevation in total CK and CKMB (CK-2) so as to mask elevations subsequent to intraoperative myocardial infarction.

V. Intended Use

A. Intended Use

The CARESIDE™ CKMB cartridge is intended for *in vitro* diagnostic use in conjunction with the CARESIDE *Analyzer*™ to quantitatively measure CK-MB activity in anti-coagulated whole blood, serum or plasma.

B. Indications for Use

This product is indicated for use in the diagnosis and treatment of patients with myopathic disorders including myocardial infarction, myocarditis, Duchenne's muscular dystrophy, polymyosititis, and rhabdomyolysis.

VI. Technological Characteristics

A. Similarities

	CARESIDE™ CKMB	Vitros CKMB DT Slides
Intended Use	Primarily to aid in the diagnosis and treatment of patients with myopathic disorders including myocardial infarction, myocarditis, Duchenne's muscular dystrophy, polymyositits, and rhabdomyolysis.	Same
Indications	For *in vitro* diagnostic use. For professional laboratory: not for point of care or physician office laboratory use.	For *in vitro* diagnostic use.
Measurement	Quantitative	Same
Method Principle	Dry film immunoinhibitory method using reflectance photometry for signal detection.	Same
Specimen dilution	Not required	Same
Key Materials	Goat anti-human CK-M polyclonal antibody	Goat anti-human CK-M polyclonal antibody
Detector	Reflectance (570 nm)	Reflectance (680 nm)
Test time	Approximately 4 minutes warm-up (on-board) plus 5 minutes test time.	15 minutes slide warm-up (off-line) plus 5 minutes test time.
Sample Type	Anti-coagulated whole blood, serum, or plasma	Serum and Plasma
Specimen volume	8.5 µl test volume (85 ± 15 µl applied volume)	10 µl
Calibration	Calibration information bar-coded on each cartridge. Calibration information may change with each lot.	Run Vitros DT II calibrators whenever a new slide lot is used or when necessary.
Quality Control	2 levels	Same
Reporting Units	U/L	Same
Reaction Temp.	37 °C	Same

B. Differences

	CARESIDE™ CKMB	Vitros CKMB DT Slides
Accurate pipetting	Not required	Required
Reagent pre-warming	Not required	Required

C. Comparative Performance Characteristics

	CARESIDE™ CKMB	Vitros CKMB DT Slides
Detection limit	5 U/L	1 U/L
Reportable range	5 to 300 U/L	1 to 300 U/L
Accuracy	Mean recovery 103%	Not provided
Precision	Total CV, 147 U/L, 10%	Total CV, 105 U/L, 4%
Reference Method	Electrophoresis for % CKMB in combination with kinetic spectrophotometric determination of total CK	Not provided
Method comparison	CARESIDE™ = 1.00 (Paragon) – 8.9 U/L, r = 0.98	
Linearity	Linearity yielded slope and correlation coefficient within acceptable limits.	Not provided
Interference	No significant interference observed at tested concentration of interferent: Ascorbic acid 5 mg/dL Bilirubin 20 mg/dL	Various, see package insert

D. Conclusion

The nonclinical and clinical data provided demonstrate that the CARESIDE™ CK-MB product is as safe, effective, and performs as well as or better than the legally marketed predicate device

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 19 1999

Kenneth B. Asarch, Pharm. D., Ph.D.
Vice President, Quality Systems/
Regulatory Affairs
Careside Inc.
6100 Bristol Parkway
Culver City, California 90230

Re: K990434
Trade Name: CARESIDE™ CKMB
Regulatory Class: II
Product Code: JHS
Dated: January 29, 1999
Received: February 11, 1999

Dear Dr. Asarch:

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 (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

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

VI. INDICATIONS FOR USE

510(k) Number: K990434

Device Name: CARESIDE™ CKMB

Indications for use: For *in vitro* diagnostic use with the CARESIDE *Analyzer*™ to measure CK-MB from whole blood, serum or plasma specimens to aid in the diagnosis and treatment of patients with myopathic disorders including myocardial infarction, myocarditis, Duchenne's muscular dystrophy, polymyositis, and rhabdomyolysis.

Dan Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K990434

(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)