BIO-RAD Bio-Rad Laboratories

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K963018

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SUMMARY OF SAFETY AND EFFECTIVENESS

Submitter:

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Contact Person:

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Date Prepared:

July 25, 1996

Product Trade Name:

Bio-Rad Serum Proteins by Capillary Electrophoresis

Common Name:

SPCE

Classification Name:

Protein, Electrophoretic, Protein Fractionation, 75CEF

Predicate Devices

1. Paragon® SPE kit, Beckman Instruments K802592
2. Paragon CZE™ 2000 Clinical Capillary Electrophoresis System, Beckman Instruments, K953077
3. Clinical Data Management System, Bio-Rad Laboratories, K942451

The Bio-Rad Serum Proteins by Capillary Electrophoresis is designed for use on the Bio-Rad BioFocus Capillary Electrophoresis Unit. The analytical system, consisting of instrument, CDM software and reagent kit, provides an assay for the separation and percent determination of protein fractions in human serum.

To establish substantial equivalence to an existing device, and thus establish the safety and effectiveness of the Bio-Rad Serum Proteins by Capillary Electrophoresis kit, the Bio-Rad Serum Proteins by Capillary Electrophoresis has been compared to the Paragon® SPE kit, Beckman Instruments (K802592). A review of the intended use of each system shows them to be essentially the same in that they measure proteins in human serum. The intended use of the Bio-Rad Serum Proteins by Capillary Electrophoresis is stated as: *Bio-Rad Serum Proteins by Capillary Electrophoresis is designed for the separation and measurement of protein fractions in human serum when used with the Bio-Rad BioFocus Capillary Electrophoresis*

Unit. The intended use of the Beckman Paragon Electrophoresis Reagent Test Kit is stated as: *This reagent kit is intended for the diagnostic determination of proteins in human serum, cerebrospinal fluid and urine*.

Like the Paragon CZE™ 2000 Clinical Capillary Electrophoresis System, Beckman Instruments, (K953077), the Bio-Rad Serum Proteins by Capillary Electrophoresis "Serum Proteins by CE" (SPCE) utilizes the principle of capillary fraction electrophoresis to separate human serum proteins into five distinct bands. The separation is performed at a pH above the isoelectric point of serum proteins, imparting a net negative charge to each protein that is dependent on the difference between the separation pH and the individual protein isoelectric point. When an electric field is applied across the ends of the capillary, the negatively charged proteins and internal marker migrate toward the anode at a velocity dependent upon the ratio of mass to charge. At this pH, the internal surface of the silica capillary is highly ionized, and the presence of positively charged ions in the separation buffer results in a bulk flow of fluid towards the cathode. This electroosmotic flow (EOF) runs counter to the direction of protein migration and is stronger than the anodic movement of the proteins. As a result, the proteins' net motion is towards the detection zone near the cathodic end of the capillary. Measurement of protein absorbance at 225 nm is then achieved through a transparent section of the silica capillary.

Sample processing consists of a one step dilution of a serum sample with a diluent containing an internal marker. The prepared samples, up to 28, are then placed into the BioFocus for analysis.

A Reference Sample is included as the first sample analyzed in each tray to verify system performance. Proteins are measured, as they exit the cathodic end of the capillary, by direct absorbance of the peptide bond at 225 nm. The Clinical Data Management System (CDM), (K942451), utilizes the time versus signal data along with the internal marker, which is used to convert migration time to electrophoretic mobility, to quantitate the percentage of each of the five protein fractions.

The Beckman Paragon Electrophoresis Reagent Test Kit utilizes the principle of electrophoresis on an agaros gel support. When proteins are placed in wells on the agaros plate, they become negatively charged at the pH (8.6) of the buffer. When an electric field is applied, the proteins migrate towards the positive pole. At the end of the electrophoretic run the gel plate is place in an acetic acid-ethyl alcohol-water solution to fix the protein. The plate is removed from the acid-alcohol solution and dried. The dried plate is placed in a solution of Paragon Blue Stain. Upon removal from the stain, the plate is again washed with acid-alcohol and dried. The plate, with the bands visible, is scanned at 600 nm in a desitometer and the percentage of each of the five fractions are calculated.

The performance of the Bio-Rad Serum Proteins by Capillary Electrophoresis was evaluated for precision, measuring range, and accuracy. The precision studies were done according to NCCLS Evaluation protocol, Vol. 12, No 4, EP5-T2, Appendix C, pp 31-39. Twenty samples each of normal and abnormal control were analyzed for mean area percent. The Within-Run % CV for the normal control averaged 5.8 for the five fractions and for the abnormal control, 4.7. The Between-Day % CV for the normal control averaged 5.7 for the five fractions and for the abnormal control, 5.5. The Total % CV for the normal control averaged 7.1 for the five fractions and for the abnormal control, 6.4. The measuring range was determined to be down to 1 g/d/L

The correlation study, to determine accuracy, of Bio-Rad Serum Proteins by Capillary Electrophoresis and the Beckman Paragon Gel Elctrophoresis kit followed NCCLS Document EP9-T. The "r" for the five fractions averaged 0.813.

When comparing these two techniques, differences between them have to be considered when evaluating the correlation data. Capillary electrophoresis is not effected by protein aggregation due to gel porosity characteristics, nor by the problem of cryoprecipitation at the application point between the beta and gamma zones nor by the variability of protein staining as a means of detection. With capillary electrophoresis, absorbance detection of the peptide bond at 225 nm provides a more accurate method of relative percent quantitation. The weak correlation for the Beta fraction is consistent with literature reports concerning aggregation and precipitation of lipoproteins in agarose gels. This phenomenon is not seen with the SPCE kit.

When considering the technology differences between the two methods, it can be concluded from the correlation study and similarities of the general characteristics of the two assays (Appendix C), the Bio-Rad Serum Proteins by Capillary Electrophoresis and the Beckman Paragon Electrophoresis Reagent Test Kit are substantially equivalent. Based on the establishment of substantial equivalence, the safety and effectiveness of the Bio-Rad Serum Proteins by Capillary Electrophoresis is confirmed.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 4 1997

John W. Nelson
Manager, Regulatory Affairs
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Re: K963018
Bio-Rad Serum Proteins by Capillary Electrophoresis
Regulatory Class: I
Product Code: CEF, JQT
Dated: March 27, 1997
Received: March 31, 1997

Dear Mr. Nelson:

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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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/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

Statement of Intended Use

510(k) Number (If Known)

Device Name: Bio-Rad Serum Proteins by Capillary Electrophoresis

Indications for Use: Bio-Rad Serum Proteins by Capillary Electrophoresis is designed for the separation and measurement of protein fractions in human serum when used with the Bio-Rad BioFocus Capillary Electrophoresis Unit.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)
Concurrence of CDHR, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109)

150