K963803

Centocor

MAY 23 1997

10.0 510(K) SUMMARY CENTOCOR® CA 15-3™ RIA

Submitter Information

Address: Centocor Incorporated
200 Great Valley Parkway
Malvern, PA 19355

For information regarding this 510(k) Summary please contact, Centocor, Inc., Mr. Christopher D. Zalesky, (610) 651-6815

Summary Preparation Date: September 20, 1996

Name of the Device:

Trade/Proprietary Name: Centocor CA 15-3™ RIA

Common/Usual Name: Radioimmunoassay for the quantitative determination of DF3-defined antigen in serum or plasma

Classification Name: In accordance with FDA's reclassification order issued September 19, 1996, Docket # 95P-0136, Serum Tumor Markers, Centocor CA 15-3 RIA has been classified as a Class II device, Tumor Associated Antigen Immunoassay Systems.

Centocor, Inc.·200 Great Valley Parkway·Malvern, Pennsylvania 19355-1307·Telephone (610) 651-6000·Facsimile (610) 651-6100

Substantial Equivalence

The Centocor CA 15-3 RIA has been found to be substantially equivalent to Biomira Diagnostic's TRUQUANT BR RIA, P950011, approved by the Food and Drug Administration on March 29, 1996.

Device Description:

The Centocor CA 15-3 RIA is an *in vitro* diagnostic device based on the well established RIA "forward sandwich" principle. The device is in kit format and consists of murine monoclonal antibody 115D8-coated polystyrene beads, standards, diluent, positive control, and ^{125}I radio-labeled, murine monoclonal antibody, DF3. Antibody coated beads are incubated with a specimen or the appropriate standards and controls. During this initial incubation step, DF3 antibody-defined antigen present in the specimen are bound by the coated beads. Unbound material present in the specimen are removed by aspiration and washing. In the second step, the beads are incubated with DF3 radio-labeled with ^{125}I. The tracer detects DF3 antibody-defined antigen bound to the beads during the initial incubation step. The unbound tracer antibody is removed by washing and aspiration. The bound radioactivity is determined by counting the beads in a gamma counter. The bound radioactivity is directly proportional to the concentration of the DF3 antibody-defined antigen in the specimen. A standard curve is obtained by plotting the DF3 antibody-defined antigen concentration of the standards against the bound radioactivity.

Intended Use

The Centocor CA 15-3 RIA is an *in vitro* test for the quantitative determination of DF3 antibody-defined antigen, encoded by the MUC 1 gene, in serum and plasma of patients previously treated for stage II or stage III breast cancer. Serial test results obtained with the Centocor CA 15-3 RIA, in patients who are clinically free of disease,

should be used in conjunction with all relevant information derived from diagnostic tests, physical examination, and full medical history in accordance with appropriate patient management procedures used for early detection of recurrence.

Breast cancer is the most common malignancy among woman in the United States. It is estimated that approximately 184,000 new cases of breast cancer will be diagnosed each year and that approximately 44,000 woman will die of the disease. One of every nine woman in the U.S. will develop breast cancer and approximately 30% of woman who have this malignancy will die of the disease. Metastatic disease may be present at the time of initial diagnosis and can occur at any time following primary therapy. Up to 70% of patients with metastases will respond to systemic treatment with cytotoxic drugs or endocrine therapy; therefore, early detection of recurrence is important to patient management. The median survival following diagnosis of recurrent disease is approximately 2 years, but may range from a few months to decades.

In patients previously treated for stage II or stage III disease, early detection of recurrence cannot be readily accomplished by routine clinical or diagnostic studies alone. A circulating serum tumor marker assay, such as the Centocor CA 15-3 RIA, can be useful in the identification of these patients.

Technological Characteristics:

The Centocor CA 15-3 RIA and TRUQUANT BR RIA both utilize well established solid phase radioimmunoassay procedures for quantifying the amount of antigen in patient specimens. The Centocor CA 15-3 RIA is based on the "forward sandwich" principle. The amount of tracer bound to the assay solid phase is directly proportional to the amount of antigen present in the patient sample. The TRUQUANT BR RIA is based on the "competitive inhibition" principle. With this method, the amount of tracer bound to the solid phase is inversely proportional to the amount of antigen present in the patient sample.

Both the Centocor CA 15-3 RIA and the TRUQUANT BR RIA utilize monoclonal antibodies directed against mucinous antigens associated with carcinoma of the breast. These antigens are large molecular weight glycoproteins with O-linked oligosaccharide chains. Breast carcinoma-associated antigen, encoded by the human MUC 1 gene, is identified by several names including DF3 antibody-defined antigen, MAM 6 and milk mucin.

Performance Data

Analytical Performance in Breast Cancer Patients

Analytical performance of the CA 15-3 assay was evaluated in a study in which serum samples were obtained from 204 breast cancer patients. Each sample was analyzed using the Centocor CA 15-3 RIA and the TRUQUANT BR method. Samples were analyzed on two occasions, with both assays, using multiple product lots. The assays were compared for linear agreement using Bablock-Passing regression analysis, with the other commercial method as the reference method. The results are summarized below:

204 = Total samples tested
0.93 = Slope
-2.04 = Intercept
0.92 = Spearman's Rank Correlation

Inter and Intra Assay Precision

Twenty-four coded samples (2 sets of twelve samples) and one kit control were tested in duplicate by six laboratories using three Centocor CA 15-3 RIA kit lots on each of three days. The order of the coded samples was randomized for each day's testing. The estimates of intra-assay precision (CV_o) ranged from 5.4 to 9.4%. The estimates of inter-assay lot precision (CV_x) ranged from 7.0% to 11.5%. Samples with a mean CA 15-3

assay value around the reference value of 35 U/mL had CV_x s of in the range of 5.8% to 8.5%. Nonclinical Studies

Conclusion from Studies

The Centocor CA 15-3 RIA and the TRUQUANT BR RIA demonstrated good linear agreement and precision comparable to that claimed in the TRUQUANT BR RIA product instructions. The two products are substantially equivalent.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 23 1997

Mr. Christopher D. Zalesky
Director, Regulatory Affairs
Centocor Incorporated
200 Great Valley Parkway
Malvern, Pennsylvania 19355

Re: K963803/S2
Trade Name: Centocor CA 15-3™ RIA
Regulatory Class: II
Product Code: MOI
Dated: May 7, 1997
Received: May 8, 1997

Dear Mr. Zalesky:

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 at (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

510(k) Number (if known): K963803

Device Name: Centocor ®CA 15-3™ RIA

INDICATIONS FOR USE

The Centocor CA 15-3 RIA is an *in vitro* test for the quantitative determination of DF3 antibody-defined antigen, encoded by the MUC 1 gene, in serum and plasma.

Serial test results obtained with the Centocor CA 15-3 RIA, are useful in the early detection of recurrence in patients previously treated for stage II or stage III breast cancer, who are clinically free of disease. Early detection of recurrence cannot be readily accomplished by routine clinical or diagnostic studies alone. The use of a circulating serum tumor marker assay, such as Centocor CA 15-3 RIA, can be useful in the identification of these patients. The Centocor CA 15-3 RIA should be used in conjunction with all relevant information derived from diagnostic tests, physical examination and full medical history, in accordance with appropriate patient management procedures

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(Concurrence of CDRH, Office of Device Evaluation (ODE)

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

Prescription Use ✓
(Per 21 CFR 801.109)

or

Over-The-Counter Use ____

(Optional Format 1-2-96)