K 031393

JUN 2 4 2003

# Section 4
# Premarket Notification – 510(k)

## Bayer HealthCare
## Diagnostics Division
## ADVIA Centaur® CA 19-9 Assay

## Summary of Safety and Effectiveness

# Bayer HealthCare, Diagnostics Division
# ADVIA Centaur CA 19-9 Assay

## Summary of Safety and Effectiveness

*This Summary of Safety and Effectiveness has been prepared in accordance with the requirements of 21 CFR 807.92, to provide sufficient information to understand the basis for a determination of substantial equivalence.*

## 1. Submitter Information

Contact Person: Kenneth T. Edds, Ph.D.

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Diagnostics Division
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Date Summary Prepared: April 25, 2003

## 2. Device Information

Propriety Name: ADVIA Centaur® CA 19-9 Assay

Common Name: Immunological test for CA 19-9 Antigen (1116NS19-9 Antibody Defined Antigen)

Classification Name: Tumor Associated Antigen Immunological Test System; Calibrator

Class: II
CFR: 21 CFR 866.6010; 21 CFR 862.1150
Product Code: NIG, JIT

## 3. Predicate Device Information

Name: Fujirebio Diagnostics CA 19-9 RIA

Manufacturer:
Manufactured by: Fujirebio Diagnostics, Inc.
201 Great Valley Parkway
Malvern, PA 19355

510(k) Number: K020566

## 4. Device Description

The ADVIA Centaur CA 19-9 assay is a fully automated, two-step sandwich immunoassay using direct, chemiluminescent technology. The method utilizes a single monoclonal antibody (Mab), 116-NS-19-9, for both the Solid Phase and the Lite Reagent. The Mab is both covalently coupled to paramagnetic particles in the Solid Phase as well as labeled with acridinium ester in the Lite Reagent.

The sample and Solid Phase are first incubated at 37ºC for 7.5 minutes. This step is followed by a wash step to remove excess unbound antigen. The Lite Reagent is then reacted with the Solid Phase that is bound to CA 19-9 antigen for an additional 20-minute incubation. This two-step protocol eliminates any high-dose hook effect in this assay.

## 5. Statement of Intended Use

The ADVIA Centaur® CA 19-9 Assay is an *in vitro* immunoassay for the quantitative measurement of the CA 19-9 tumor-associated antigen, in human serum, using the ADVIA Centaur System. This assay is indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The test is useful as an aid in monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of serum CA 19-9 at some point in their disease process exceeding the median concentration determined for the apparently healthy cohort. CA 19-9 values must be interpreted in conjunction with all other clinical and laboratory data before a medical decision is determined. This assay is not intended for use on any other system.

## 6. Substantial Equivalence

The ADVIA Centaur CA 19-9 Assay is substantially equivalent to the Fujirebio Diagnostics CA 19-9 RIA predicate device cleared under K020566. Both products are based on the use of the same monoclonal antibody (Mab), 1116NS19-9, which is intended for use in the quantitative determination of the CA 19-9 tumor-associated antigen.

### (a) Technological Characteristics

The following table compares the technology features of the ADVIA Centaur CA 19-9 Assay with the Fujirebio Diagnostics CA 19-9 RIA predicate device:

| Feature | ADVIA Centaur® CA19-9 Immunoassay | Fujirebio Diagnostics CA 19-9 RIA (Predicate Device) |
|---|---|---|
| Intended Use | Quantitative determination of CA 19-9 tumor-associated antigen | Quantitative determination of CA 19-9 tumor-associated antigen |
| Indication for Use | An aid in the management of patients diagnosed with cancers of the exocrine pancreas | An aid in the management of patients diagnosed with cancers of the exocrine pancreas |
| Assay Principle | Chemiluminescence immunoassay | Radioimmunoassay |
| Sample Type | Human serum | Human serum or plasma |
| Sample Volume | 75 µL | 100 µL |

| Feature | ADVIA Centaur® CA19-9 Immunoassay | Fujirebio Diagnostics CA 19-9 RIA (Predicate Device) |
|---|---|---|
| Calibrator | CA 19-9 Calibrator set (2 levels) | CA 19-9 Standard set (6 levels including 0) |
| Controls | Tumor Marker Plus 1, 2 Control set | Defibrinated human plasma containing 2 levels of CA 19-9 |
| Instrument | ADVIA Centaur System, a fully automated, random-access immunoassay analyzer | Manual method or semi-automated with commercially available rinsing/aspiration systems |
| Measuring Range | 1.2 – 700 Units/mL | 0.9 – 240 Units/mL |

## (b) Performance Characteristics

The following table compares the performance characteristics of the ADVIA Centaur CA 19-9 assay with the Fujirebio Diagnostics CA 19-9 RIA predicate device:

| Feature | Bayer ADVIA Centaur® CA 19-9 Immunoassay | Fujirebio Diagnostics CA 19-9 RIA (Predicate Device) |
|---|---|---|
| Precision | • Within-run 4.3 – 11.3 %CV from 7.2 – 386.7 Units/mL<br>• Total 5.5 – 14.5 %CV from 7.2 – 386.7 Units/mL | • Values for duplicates should be within 15% of the mean (except for 0 standard0 |
| Hook Effect | No high dose effect up to 5,800,000 Units/mL | None up to 1,250,000 Units/mL |
| Analytical Sensitivity | 1.2 Units/mL | 0.9 Units/mL |
| Limitations/Warning/Pre-cautions | • This test has been evaluated with serum.<br>• No interference from hemoglobin up to 1200 mg/dL<br>• No interference from triglycerides up to 3500 mg/dL<br>• No interference from bilirubin up to 60 mg/dL<br>• No interference from human serum albumin up to 14 g/dL<br>• No interference from commonly used pharmaceutical drugs.<br>• Patients known to be genotypically negative for the Lewis blood group antigen will be unable to produce the CA 19-9 antigen even in the presence of malignant tissue.<br>• Results should always be assessed in conjunction with the patient's medical history, clinical evaluation and other diagnostic procedures. | • This test has been evaluated with serum and plasma (using different anticoagulants). However, it is recommended that if the specimen type is changed during patient monitoring, the patient should be re-baselined to negate any potential biases due to specimen type.<br>• The assay should not be performed on clotted, icteric hemolyzed or lipemic samples.<br>• No interference from commonly used pharmaceutical drugs.<br>• Patients known to be genotypically negative for the Lewis blood group antigen will be unable to produce the CA 19-9 antigen even in the presence of malignant tissue.<br>• Results should always be assessed in conjunction with the patient's medical history, clinical evaluation and other diagnostic procedures. |

## (c) Clinical Concordance

The following two 2x2 tables compare the clinical concordance of the ADVIA Centaur CA 19-9 Assay (test device) and the Fujirebio Diagnostics CA 19-9 RIA (predicate device) with a change in a patient's CA 19-9 value relative to disease progression.

Monitoring of Pancreatic Cancer Patients for Changes in Disease Status: Correspondence of Serial CA 19-9 Changes as Measured by the ADVIA Centaur CA 19-9 Assay (Test Device) and Clinical Status (Per-Visit Analysis).

| | | *Change in Disease State* | |
|---|---|---|---|
| ***Change in CA 19-9*** | ***Progression*** | ***No Progression*** | ***Total*** |
| ***> 15% increase*** | 39 | 27 | 66 |
| ***≤ 15% increase*** | 18 | 47 | 65 |
| ***Total*** | 57 | 74 | 131 |

Concordance = (39+47)/ 131 = 65.7% (95% CI of 54.9% to 76.3%)

Predictive Value (No Progression) = 47/74 = 63.5% (95% CI of 52.9% to 77.4%)

Predictive Value (Progression) = 39/57 = 68.4% (95% CI of 56.6% to 80.1%)

Monitoring of Pancreatic Cancer Patients for Changes in Disease Status: Correspondence of Serial CA 19-9 Changes as Measured by the Fujirebio Diagnostics CA 19-9 RIA (Predicate Device) and Clinical Status (Per-Visit Analysis).

| | | *Change in Disease State* | |
|---|---|---|---|
| ***Change in CA 19-9*** | ***Progression*** | ***No Progression*** | ***Total*** |
| ***> 20% increase*** | 37 | 19 | 57 |
| ***≤ 20% increase*** | 20 | 55 | 74 |
| ***Total*** | 55 | 74 | 131 |

Concordance = (37+55)/ 131 = 70.2% (95%CI of 59.5% to 80.9%)

Predictive Value (No Progression) = 55/74 = 74.3% (95% CI of 64.3% to 83.8%)

Predictive Value (Progression) = 37/57 = 64.9% (95% CI of 52.9% to 77.1%)

For 360 samples in the assay range of 1.2 - 700 Units/mL, the relationship of the ADVIA Centaur CA 19-9 Assay to the Fujirebio Diagnostics CA 19-9 RIA is described by the following equation (as determined with a Passing-Bablock Regression):

ADVIA Centaur CA 19-9 = 0.97 (Fujirebio RIA) + 0.13 Units/mL

The correlation coefficient (r) is 0.88.

| | **Coefficient** | **95% CI** |
|---|---|---|
| **Intercept** | 0.127 | -1.234 to 1.970 |
| **Slope** | 0.972 | 0.914 to 1.032 |

The non-clinical and clinical data presented herein demonstrate substantial equivalence of the ADVIA Centaur CA 19-9 Assay to the FDA-cleared Fujirebio Diagnostics CA 19-9 RIA.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 24 2003

Kenneth T. Edds, Ph.D.
Manager Regulatory Affairs
Bayer HealthCare
Diagnostics Division
511 Benedict Avenue
Tarrytown, New York 10591-5097

Re: k031393
Trade/Device Name: ADVIA Centaur® CA 19-9 Assay
Regulation Number: 21 CFR § 866.6010
Regulation Name: Tumor Associated Antigen Immunological Test System; Calibrator
Regulatory Class: II
Product Code: NIG, JIT
Dated: May 2, 2003
Received: May 5, 2003

Dear Dr. Edds:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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 (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer 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
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K031393

Device Name: ADVIA Centaur® CA 19-9 Assay

**Indications for Use:**

The ADVIA Centaur® CA 19-9 Assay is an *in vitro* immunoassay for the quantitative measurement of the CA 19-9 tumor-associated antigen, in human serum, using the ADVIA Centaur System. This assay is indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The test is useful as an aid in monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of serum CA 19-9 at some point in their disease process exceeding the median concentration determined for the apparently healthy cohort. CA 19-9 values must be interpreted in conjunction with all other clinical and laboratory data before a medical decision is determined. This assay is not intended for use on any other system.

(PLEASE DO NOT WRITE BELOW THIS LINE--CONTINUE ON ANOTHER PAGE, IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109) (Optional Format 1-2-96)

J P Reeves for S. Baumgart
Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K031393