Summary of Safety and Effectiveness Information Supporting a Substantially Equivalent Determination

K030754

1. Submitter Information

Submitter: A/C Diagnostics Division
AntiCancer Inc.
7917 Ostrow Str.
San Diego, California 92111
Phone: (858)654-2555
FAX: (858)268-4175
e-mail: all@anticancer.com

Contact Person: Yuying Tan, M.D.
Research Manager
AntiCancer Inc.

Date of Summary Preparation: February 18, 2003

2. Device Information

Device Name: **A/C Enzymatic Homocysteine Assay**

Classification Name: Homocysteine Assay
Class: II
Product Code: LPS

3. Predicate Device Information

Device Name: Bio-Rad Homocysteine by HPLC
Bio-Rad Laboratories
Diagnostics Group
4000 Alfred Nobel Drive
Hercules, California 94547

510(k) Number: K993107

4. Information of Manufacturer

Manufacturer: Bioserv Corporation
5340 Eastgate Mall
San Diego, CA 92121
Telephone: (858) 450-3123
FAX: (858) 450-0785

FDA establishment registration number: US FDA 2027352

Contact Person : Mary Richardson
Quality Assurance Manager
Bioserv Corporation

5. Statement of Intended Use

- The A/C Enzymatic Homocysteine Assay is intended for the quantitative determination of total homocysteine (tHCY) in human plasma or serum.
- The device can assist in the diagnosis and treatment of patients suspected of having hyperhomocysteinemia.
- The A/C Enzymatic Homocysteine Assay Kit is only for *in vitro* diagnostic use.

6. Description of Device

The A/C Enzymatic Homocysteine Assay is calibrated with A/C Enzymatic Homocysteine Assay Calibrators. The A/C Enzymatic Homocysteine Assay is assayed for the verification of the accuracy and precision on the Hitachi 912 Automatic Analyzer.

The A/C Enzymatic Homocysteine Assay measures tHCY. The principle of the assay is that recombinant homocysteinase (rHCYase) produces hydrogen sulfide (H_2S) from tHCY, which is quantified by use of N,N-dibutyl phenylene diamine (DBPDA), the combination of which forms a chromophore.

The A/C Enzymatic Homocysteine Assay on the Hitachi 912 Automatic Analyzer used four reagents, a number compatible with implementation on the Hitachi 912 Automatic Analyzer. We used 30 µL of EDTA plasma in a dithiothreitol (DTT) reduction reaction (1 mmol/L DTT, 0.2% Triton X-100 in 40 mmol/L sodium phosphate buffer [pH 8.3]) for 1.5 minutes to release bound homocysteine. The rHCYase reaction (0.05 mg/ml in 40 mmol/L sodium phosphate buffer [pH 8.3] with 20 µmol/L pyridoxal 5-phosphate [PLP]) is then run for 3.5 minutes. The DBPDA chromophore (12.5 mmol/L DBPDA in 1.5 N H_2SO_4) is then added and 5 minutes later, an oxidant, potassium ferricyanide (5 mmol/L $K_3Fe(CN)_6$ in 10 mmol/L sodium phosphate

buffer [pH 7.6]), is added. Five minutes after addition of oxidant, the end-points are read at absorbances of 700 and 660 nm. As the assay is based on an increase in absorbance over baseline, no blank without enzyme was used. The detection limit of the assay is 1.5 µmol/L defined by quantification of a serial dilution of a plasma sample of tHCY diluted to 0.77 µmol/L. The limit of quantification is defined as the lowest concentration measured having a CV <20%. The linear range extends to at least 80 µmol tHCY/L as determined by measuring varying amounts of homocysteine in phosphate buffered saline.

The within-run imprecisions (CV) run over 8 repeats were 4.8% at 8.9 µmol/L tHCY; 3.0% for 14.9 µmol/L tHCY; and 4.5% for 25 µmol/L tHCY. Between-assay imprecisions (CV) over 10 days were 7.8% for 8.8 µmol/L tHCY; 5.9% for 15 µmol/L tHCY; and 4.9% for 25 µmol/L tHCY. These imprecisions are with in ranges reported for currently-used assays including the Bio-Rad HCY assay on HPLC, which is used as a comparison method in the present study.

The results showed that L-cysteine (L-CYS) in the physiological concentrations (0-200 µmol/L) had less than 10% interference and L-methionine (L-MET) in the physiological concentrations (0-200 µmol/L) had no interference in the A/C Enzymatic Homocysteine Assay on the Hitachi 912 Automatic Analyzer.

The A/C Enzymatic Homocysteine Assay on the Hitachi 912 Automatic Analyzer is a four-step reaction. The total assay takes 15 minutes, and the through-put is 360 tests per hour.

7. Method Comparison

To establish equivalence to an existing device, and thus establish the safety and effectiveness, the A/C Enzymatic Homocysteine Assay on Hitachi 912 Automatic Analyzer is compared to the Bio-Rad Homocysteine by HPLC (k 993107).

We assayed 121 plasma samples with the A/C Enzymatic Homocysteine Assay on the Hitachi 912 Automatic Analyzer (y) and with the Bio-Rad Homocysteine Assay by HPLC (x). The regression equation was $y = 0.98 + 1.90$ ($r = 0.977$). The mean difference (SD) between the A/C Enzymatic Homocysteine Assay and the Bio-Rad Homocysteine by HPLC was -1.62 µmol/L (SD=2.33). Differences were not significantly correlated with homocysteine concentration (Pearson $r = 0.12$, $p = 0.185$).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 11 2003

Yuying Tan, M.D.
Research Manager
AntiCancer Inc.
A/C Diagnostics Division
7917 Ostrow Street
San Diego, CA 92111

Re: k030754
Trade/Device Name: A/C Enzymatic Homocysteine Assay
Regulation Number: 21 CFR 862.1377
Regulation Name: Urinary homocystine (non-quantitative) test system
Regulatory Class: Class II
Product Code: LPS
Dated: May 15, 2003
Received: May 16, 2003

Dear Dr. Tan:

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

Appendix-6

K030754

Indications for Use:

- **The A/C Enzymatic Homocysteine Assay is intended for the quantitative determination of total homocysteine (tHCY) in human plasma or serum.**
- **The device can assist in the diagnosis and treatment of patients suspected of having hyperhomocysteinemia.**
- **The A/C Enzymatic Homocysteine Assay is only for *in vitro* diagnostic use.**

✓ prescription use

Division Sign-Off for Jean Cooper

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) 030754