

K980907

OCT 16 1998

**510(k) Summary**

**Axis® Homocysteine Enzyme Immunoassay**

## 510(k) Summary

### Axis<sup>®</sup> Homocysteine Enzyme Immunoassay

#### Summary of Safety and Effectiveness Information Supporting a Substantially Equivalent Determination

The Axis<sup>®</sup> Homocysteine Enzyme Immunoassay is designed for the quantitative determination of total homocysteine in plasma or serum.

Homocysteine is a thiol-containing amino acid produced by the intracellular demethylation of methionine. Homocysteine is metabolized to either cysteine or to methionine. In the vitamin B<sub>6</sub> dependent trans-sulphuration pathway homocysteine is irreversibly catabolised to cysteine. A major part of homocysteine is remethylated to methionine, mainly by the folate and cobalamin-dependent enzyme methionine synthase. Homocysteine accumulates in the cell and is exported to the circulation when these reactions are impaired. Homocysteine circulates in plasma mostly in its oxidized form bound to proteins and is measured as total homocysteine (tHcy) the sum of free and protein bound fractions.

In the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay, protein bound homocysteine is reduced to free homocysteine, enzymatically converted to S-adenosyl-L-homocysteine (SAH), and detected in competitive immunoassay with monoclonal anti-SAH antibody.

There are several 510(k) cleared methods for measurement of amino acids<sup>1,2,3</sup>. All these methods are based on HPLC separation and either traditional post-column derivitization (LKB, Beckman) or pre-column derivitization (Waters). Homocysteine can be analyzed using a traditional HPLC method with post-column derivitization. For example, Poele-Pothoff<sup>4</sup> et al used a traditional system with 3 hours analysis for this purpose (LKB analyzer). Sera were reduced using dithiotreitol, then proteins were precipitated as would normally be done for this instrument. Candito<sup>5</sup> et al also published an analysis of homocysteine using a Beckman Amino Acid Analyzer, after reduction with dithiotreitol. Both of these methods are based on earlier work by Andersson<sup>6</sup>, which used a modified separation on an amino acid analyzer.

To establish substantial equivalence to an existing device, and thus establish the safety and effectiveness of the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay, the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay was compared to the University of Bergen Homocysteine by HPLC method<sup>7</sup>. This method uses pre-column derivitization and permits rapid analysis. In the work of Poele-Pothoff, a similar pre-column method was compared to an amino acid analyzer method and was shown to give an excellent correlation.

The performance of the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay was evaluated for precision, measuring range, accuracy and limit of quantification. The precision studies were done according to NCCLS Evaluation protocol, Vol. 12, No. 4, EP5-T2. Using this protocol, precision of the system was determined using Low, Medium and High controls. The Within-run %CV for the Low was 7.3%, for the Medium 6.8%, and for the High 5.2%. Total precision was

9.3% for the Low, 8.1% for the Medium and 7.1% for the High. The assay is linear within the measuring range: 2 - 50  $\mu\text{mol/L}$  and has a limit of homocysteine quantification of  $< 0.5 \mu\text{mol/L}$ .

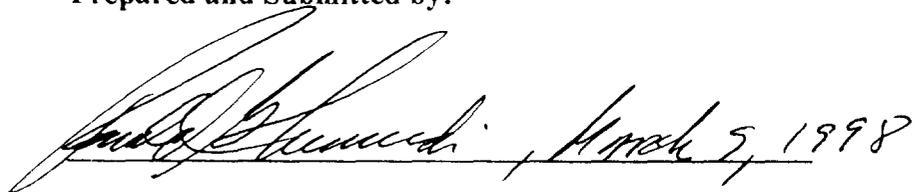
A correlation study, to determine accuracy of the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay, was done against the University of Bergen Homocysteine by HPLC method. The study followed NCCLS Document EP9-T. The  $r^2$  for the correlation was 0.94, the Slope was 0.94, and the Y-Intercept was - 0.09.

When considering an excellent correlation between the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay and the University of Bergen Homocysteine by HPLC method, it can be concluded that the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay is substantially equivalent to the HPLC method. Based on the establishment of substantial equivalence, the safety and effectiveness of the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay is confirmed.

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1. *LKB Instruments Inc. 4150 Alpha Amino Acid Analyzer. 510(k) Number: K820415, 02/11/82.*
  2. *Beckman Instruments Inc. System 6300 Series High Performance Amino Acid Analyzer. 510(k) Number: K92093, 11/16/92.*
  3. *Waters Chromatography Division. Waters Pico Tag Chem Pack. Free Amino Acid Analysis Kit. 510(k) Number: K943978, 05/02/95.*
  4. *Poele-Pothoff et al, Ann. Clin. Biochem., 1995, 32: 218-220.*
  5. *Andersson et al, Scand. J. Clin Lab Invest, 1989, 49: 445-449.*
  6. *Candito et al, Journal of Chromatography, 1997, 692: 213-216.*
  7. *Fiskerstrand et al, Clin. Chem. 1993, 39: 263-271.*

In conclusion, these data demonstrate that the Axis<sup>®</sup> Homocysteine Enzyme Immunoassay is as safe and effective as, and is substantially equivalent to the Beckman System 6300 Series High Performance Amino Acid Analyzer, K 92093

**Prepared and Submitted by:**



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**for AXIS BIOCHEMICALS,**  
**NORWAY**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

OCT 16 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Ronald G. Leonardi, Ph.D.  
President  
R & R Registrations  
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San Diego, California 92196-2069

Re: K980907  
AXIS® Homocysteine Enzyme Immunoassay  
Regulatory Class: I & II  
Product Code: JJX, LPS, DFC  
Dated: September 10, 1998  
Received: September 11, 1998

Dear Dr. Leonardi:

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 (Pre-market 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 pre-market 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.

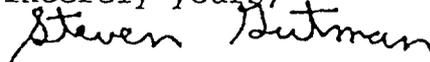
Page 2

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 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): K980907

Device Name: Axis® Homocysteine Enzyme Immunoassay

Indications for Use:

The Axis Homocysteine Enzyme Immunoassay is intended for the quantitative measurement of total L-homocysteine in human serum or plasma.

The device can assist in the diagnosis and treatment of patients suspected of having hyperhomocysteinemia and homocysteinuria.

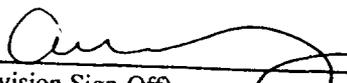
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Concurrence of CDHR, Office of Device Evaluation (ODE)

Prescription Use ✓  
(Per 21 CFR 801.109)

OR Over-The-Counter Use \_\_\_\_\_

(Optional Format 1-2-96)

  
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(Division Sign-Off)  
Division of Clinical Laboratory Devices  
510(k) Number K980907