DEC 21 199

K992502

9.0 510(k) Summary

The Axis® %CDT Turbidimetric Immunoassay (TIA) is designed for the quantitative determination of carbohydrate deficient transferrin (CDT) in serum.

Serum transferrin is a glycoprotein with a molecular weight of about 80kD, which comprises a single polypeptide chain with two N-linked polysaccharide chains. These polysaccharide chains are branched with terminal sialic acid residues. Human transferrin occurs in isoforms with different levels of sialylation. There appear to be at least six such isoforms, from penta to asialo transferrin.

Daily intake of alcohol exceeding 60 grams of ethanol for periods longer than two weeks may result in elevated levels of CDT.

The Axis® %CDT is a heterogeneous immunoassay with column separation followed by turbidimetric measurement. Serum transferrin in the sample is saturated with Fe^{3+}. The mixture is applied to an ion-exchange column. Due to the different amounts of sialic residues on transferrin, the isoforms carry different charges and are separated in the column. The CDT isoforms are eluted. The CDT content of the collected eluate is determined by turbidimetric measurement.

The eluted CDT isoforms form immune complexes with anti-transferrin antibodies. Total transferrin content of the sample is determined separately, using the same anti- transferrin antibodies. The measurements are evaluated using a calibration curve, and the Axis® %CDT value is calculated.

The substantial equivalence, safety and efficacy of the Axis® %CDT TIA, was compared to gamma glutamyl transferase (GGT) in the study CT-C8001.

The issues addressed in this study were clinical distribution of Axis® %CDT in social drinkers and in chronic heavy drinkers, the relationship between Axis® %CDT and GGT, the sensitivities and specificities of Axis® %CDT at various cut-off levels, and the performance of CDT versus GGT for the identification of chronic heavy alcohol use.

The study demonstrated that chronically heavy drinking individuals have higher CDT levels than socially drinking individuals, and that females and males do not have substantially different Axis® %CDT levels which suggests that a common cut-off could be utilised for males and females. The correlation between Axis® %CDT and GGT were low and not significant which is consistent with previous reports in the literature. Sensitivity and specificity at a reference value of 5%CDT was 0.70 and 0.93 for males and 0.55 and 0.91 for females respectively. 5% is close to the 95 % percentile value (5.1%) observed in the social drinking (normal population) group. The Axis® %CDT level among females is slightly higher than among males. Visual inspection of Receiver Operating Characteristics (ROC) curves comparing Axis® %CDT and GGT for both genders, separately and together suggests that for all subjects there is no difference in the performance characteristics for Axis® %CDT and GGT. This was confirmed by exactly identical areas under the curves for both biomarkers.

For male subjects area under the curve suggests slightly better performance for CDT while in females a better performance was seen by GGT.

Precision studies were done according to NCCLS document EP5-T2. Precision of the system was determined using low and high controls. Within-run CV for low and high control was 4.8% and 2.7% respectively and total precision was 6.4% and 3.4% respectively. Limit of detection (LOD) for the Axis® %CDT assay is 1.0 mg/L transferrin and the limit of quantification (LOQ) is 1.0 mg/L CDT and 1.5 mg/L total transferrin. The assay is linear within the measuring range; 0 – 50 mg/mL. Accuracy of the assay was determined by comparing Axis® %CDT microtiter version to HPLC %CDT. Correlation coefficient, r^2, was 0.96, slope was 1.12 and Y-Intercept was –0.15. %CDT is calculated by an equation including measured concentration of transferrin (mg/L) in the eluate and in the total transferrin sample, justified by dilution factors. Effect on quantification of Axis® %CDT TIA by endogenous interfering substances were tested. Haemoglobin and bilirubin showed less than 10% interference, while lipid concentrations above 10g/L showed interference above 10%. Significantly higher %CDT values were observed in plasma compared to serum and drug interference seemed to have no effect on CDT level. A critical Hook effect occurs at concentrations above 100mg/L total transferrin (TT), however this has no consequences on the Axis® %CDT assay since even extreme TT values in humans are far below 100mg/L. Antibody used in the assay is a rabbit, gamma globulin fraction purified by ammonium sulfate precipitation. The Axis® %CDT assay is influenced by temperature. When low and high controls were eluted at three different temperatures (18°, 25° and 30.5°C) the %CDT concentration for low control inclined from 2.5% to 3.5% to 4.9% and for high control from 8.3% to 9.5% to 11.2%. Calibrator value assignment is controlled against master-lot calibrators. Control value assignment is set for each lot by internal and external testing.

Conclusion

When considering the above noted correlation between Axis® %CDT TIA and the GGT assay, and with reference to the documented advantage of CDT to GGT in particular patient groups in Substantial Equivalence section, it can be concluded that the Axis® %CDT TIA is substantially equivalent to GGT. Thus safety and effectiveness of CDT is confirmed.

RONALD G. LEONARDI, Ph. D. July 23, 1999

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 21 1999

Axis Biomedical , ASA
c/o Ronald G. Leonardi, Ph.D.
R & R Registrations
P.O. Box 262069
San Diego, California 92196-2069

Re: K992502
Trade Name: AXIS % CDT Turbidimetric Immunoassay
Regulatory Class: I reserved
Product Code: NAO
Dated: October 19, 1999
Received: October 20, 1999

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 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). 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 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 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/dsma/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): K992502

Device Name: Axis® %CDT Turbidimetric Immunoassay

Indications for Use:

The Axis ® %CDT Turbidimetric Immunoassay (TIA) is intended for the quantitative measurement of carbohydrate deficient transferrin (CDT) in human serum, as a tool to identify possible chronic heavy alcohol consumption.

The Axis ® %CDT Turbidimetric Immunoassay is designed for the quantitative determination of carbohydrate deficient transferrin (CDT) in human serum.

Serum transferrin is a glycoprotein with a molecular weight of about 80kD, which comprises a single polypeptide chain with two N-linked polysaccharide chains. These polysaccharide chains are branched with terminal sialic acid residues. Transferrin is an iron-transporting protein. Human transferrin occurs in isoforms with different levels of sialylation. There appear to be at least six such isoforms; penta-, tetra-, tri-, di-, mono- and asialo transferrin.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K992502

(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)