510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number: K031924

B. Analyte: Vitros Chemistry products dHDL

C. Type of Test: The Vitros dHDL quantitatively measures HDL Cholesterol in plasma and serum.

D. Applicant: Neil Greenberg, Ph.D. , Ortho-Clinical Diagnostics**,** Regulatory Affairs, 100 Indigo Creek, Rochester, NY 14626-5101

E. Proprietary and Established Names: Vitros 5,1 FS Chemistry Systems
Vitros Chemistry Products dHDL Reagent Pack, Vitros Chemistry Products Calibrator Kit 19, Vitros Chemistry Products FS Calibrator.
Common Names – Clinical Chemistry Analyzer, HDL Cholesterol assay

F. Regulatory Information:

1. Regulation section: Discrete photometric analyzer: 21 CFR 862.2160 Lipoprotein assay: 21 CFR 862.1475, Calibrator 21 CFR 862.1150

2. Classification: Analyzer and HDL Cholesterol Assay Class I, Calibrator Class II

3. Product Code: Clinical Chemistry Analyzer JJE, dHDL Cholesterol Assay LBR, Calibrators JIT

4. Panel: 75 for all

G. Intended Use:

1. Indication(s) for use: The VITROS 5,1 FS Chemistry System is intended for use in the *in vitro* quantitative measurements of a variety of analytes of clinical interest, using both VITROS Chemistry Products Slides (colorimetric endpoint, rate, ion-selective electrode, and immunorate methods) and VITROS Chemistry Products MicroTip liquid reagents (spectrophotometric and spectrophotometric immunoassay methods.)
The VITROS Chemistry Products dHDL Reagent Pack, VITROS Chemistry Products Calibrator Kit 10 is for in vitro diagnostic use only. The dHDL quantitatively measures HDL Cholesterol in plasma and serum. HDL cholesterol is used to evaluate the risk of developing coronary artery disease. The risk of CHD increases with lower HDL cholesterol concentrations.

2. Special condition for use statement(s): N/A

3. Special instrument Requirements: The VITROS dHDL Chemistry pack is used with the VITROS 5,1 FS Chemistry System.

H. Device Description: The VITROS 5,1 FS Chemistry System is a random access, fully automated clinical chemistry analyzer intended for use in the *in vitro* determination of a variety of general chemistries, therapeutic drugs, drugs of abuse, proteins and other chemistries of clinical interest in biological fluids such as serum, plasma, urine and cerebral spinal fluid (sample type is chemistry dependant) The system has been designed for high volume clinical *in vitro* diagnostic applications. The analyzer operates in conjunction with reagents, calibrators and controls designed for use with the system. Major components include a command center/operator interface, a sampling center, a disposable tip processing center, the VITROS Chemistry Slide General Chemistry Center, and the VITROS MicroTip Special Chemistry processing center.

The VITROS Chemistry MicroTip range of products are combined with the VITROS 5,1 FS Chemistry System to perform the VITROS dHDL assay for HDL Cholesterol (reagent and calibrators). The VITROS Chemistry Products dHDL Reagent Pack, VITROS Chemistry Products Calibrator Kit 19 is for in vitro diagnostic use only. The dHDL quantitatively measures HDL Cholesterol in plasma and serum. HDL cholesterol is used to evaluate the risk of developing coronary artery disease. The risk of CHD increases with lower HDL cholesterol concentrations.

I. Substantial Equivalence Information:

1. Predicate device name(s): For the Analyzer – VITROS 950 Chemistry System K946090 & Bayer ADVIA 1650 Chemistry System K990346

For the dHDL assay Bayer Direct HDL Cholesterol II K982341

2. Predicate K number(s): For the Analyzer – VITROS 950 Chemistry System K946090 & Bayer ADVIA 1650 Chemistry System K990346

For the dHDL assay and calibrators - Bayer Direct HDL Cholesterol II K982341

3. Comparison with predicate:

DEVICE	PREDICATE	
A. Similarities		
VITROS 5,1 FS Chemistry System Technology/Methodology – Colorimetric, Poteniometric, Rate, Immunorate Sample Containers – Cups, primary collection tubes Selective/Discrete testing, STAT capability, Sample ID input, Online QC,	Vitros 950 Technology/Methodology – Colorimetric, Poteniometric, Rate, Immunorate Sample Containers – Cups, primary	Bayer ADVIA Technology/Metodology – Colorimetric, Poteniometric, Rate, Immunorate Sample Containers – Cups, primary

Test Panels, Bi-Directional Interface, Primary Container Sampling, Reagent Barcodes, Calibration display, TEST modes, Maintenance checks SW, Subsystem performance checks SW, Environmental Monitoring, Result Reporting, Patient results stored on board, S/W QC package, CLOT detection, Level sense (sample), Operator Interface VITROS dHDL Assay Basic Principle, Reagents, sample type, incubation temp.	collection tubes Selective/Discrete testing, STAT capability, Sample ID input, Online QC, Test Panels, Bi-Directional Interface, Primary Container Sampling, Reagent Barcodes, Calibration display, TEST modes, Maintenance checks SW, Subsystem performance checks SW, Environmental Monitoring, Result Reporting, Patient results stored on board, S/W QC package, CLOT detection, Level sense (sample), Operator Interface VITROS dHDL Assay Basic Principle, Reagents, sample type, incubation temp.	collection tubes Selective/Discrete testing, STAT capability, Sample ID input, Online QC, Test Panels, Bi-Directional Interface, Primary Container Sampling, Reagent Barcodes, Calibration display, TEST modes, Maintenance checks SW, Subsystem performance checks SW, Environmental Monitoring, Result Reporting, Patient results stored on board, S/W QC package, CLOT detection, Level sense (sample), Operator Interface
B. Differences		
Throughput 845 tests per hour Throughput 370 samples per hour	752 t.p.h. 300 s.p.h.	1650 t.p.h. 1200 s.p.h.
Technology Chemistry slides – Colorimetric, Poteniometric, Rate, and Immunorate. Micro tip reagents	N/A	N/A
Load Master Curve Info – CD-ROM	3.5” diskette	User config
Load Assay Protocol info – CD-ROM	User config	User Config
Display Cal curve – No	No	Yes
Electrolyte Reference fluid – 800 10ul drops	800 10ul drops	None
On-Analyzer sample capacity 150 routine, 10 STAT	40	200

Sample Status screen – No	Yes	Yes
Sample usage per assay (assay dependant) – 2 – 12ul	5 – 11ul	2 – 30ul
Waste Capacity - Slides 3,780, 1,145 VersaTips, 140 Vitros FS MicroTips, 3 MicroTip trays, 100 Vitros FS cuvettes	None stated	Requires drain with 6.8 gph flow rate.
Minimum Sample volume (worst case) – Microsample cup 30ul + 11ul per assay for up to 6 assays, 100ul + 11 per assay for 7 or more assays	Same	Sample cup 30ul + 50ul per assay
VITROS dHDL assay		
Test type – Multi point rate		2 – point rate
Instrumentation – Vitros 5,1 FS Chemistry System		Bayer ADVIA 1650
Sample volume – 3ul		5ul
Incubation time – Inc 1 = 5minutes, Inc 2 = 3.2 minutes		10 minutes

J. Standard/Guidance Document Referenced (if applicable) The standards used in this submission were, ***NCCLS Guidelines EP5A, NCCLS Guidelines EP9-A, NCCLS protocol EP6, NCCLS protocol EP6,*** and ***NCCLS protocol EP7-P.***

K. Test Principle: For the Vitro FS 5,1 Chemistry System – Chemistry Slides – Colorimetric, Poteniometric, Rate & Immunorate. MicroTip Reagents – Endpoint Colorimetric and Rate, Enzyme-coupled Immunoassay, Homogenous Turbidometric Immunoassay, Enhanced Latex ImmunoAssay

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility: The precision of Analyte Measurements on the VITROS 5,1 FS was determined using VITROS Chemistry Product Slides at various levels of activity and concentrations for a set of marker assays. The evaluation was performed on the VITROS 5,1 FS Chemistry system over a period of 10 days using one lot of slides and one instrument for each chemistry evaluated. Data were analyzed by Analysis of Variance (ANOVA). Below is a summary of the products included in the precision studies.

VITROS 5,1 FS versus VITROS 950

Analyte	Slope	Intercept	R

AST	1.00	-5.92	0.996
CREA	0.04	0.04	1.00
Phenytoin	1.02	-0.09	0.997
Na	1.00	-0.82	0.999
URIC	1.00	0.02	1.000

The comparison of the dHDL was made against a commercially available assay, Bayer Direct HDL Cholesterol II, with human patient samples. The method followed was NCCLS Guidelines EP9-A ("Method Comparison and Bias Estimation Using Patient Samples") a total of 107 serum samples were assayed using the VITROS dHDL and the Bayer ADVIA 1650 system. Samples were run in triplicate on the VITROS and a single assay was performed on each sample for the Bayer ADVIA.

Vitros dHDL Assay versus Bayer ADVIA 1650

Slope	Intercept	R
0.974	-0.0682	0.984

b. Linearity/assay reportable range: The linearity over the reportable (dynamic) range of the selected marker VITROS Chemistry slides was evaluated according to NCCLS protocol EP6. Two serum test pools were prepared with analyte concentrations near the extreme of reportable range. The reportable range of each assay is as follows – AST 3 – 750UL, CREATININE – 0.05 – 14.0mg/dl, Phenytoin 3.00 – 40.00umol/L, Sodium 75.0 – 250.0mmol/L, Uric Acid 0.50-17.00mg/dl Additionally a linearity was performed on the Vitros dHDL assay. Linearity was determined by diluting a concentrated high HDLC linearity fluid in saline, and samples were analyzed on the VITROS 5,1 FS system. The systems responses were plotted against the percent high pool and against calculated values to assess the degree to which the plotted curved conforms to a straight line. The equation of the line established was y=2.2744x-1.7229 with an R squared of 0.9985 this equation was used to plot regression concentrations. The data presented defines a linear range of the dHDL assay when run on the VITROS dHDL and established a reportable range of 2.66 to 135.64. This data supports a linearity claim of 3.0 – 100mg/dl.

c. Traceability (controls, calibrators, or method): Aliquots of sample are analyzed with an internal reference method for the particular analyte.

d. Detection limit (functional sensitivity: Detection limits were determined by measurement of the linearity range of selected marker slides. The linearity was evaluated according to NCCLS protocol EP6. Two serum pools were prepared near the extremes of reportable range, the pools were them mixed to give additional pools at intermediate

concentrations. Visual analysis determined the assay is linear across the range tested establishing a range and cutoff as listed for each marker assay. AST 3 – 750UL, CREATININE – 0.05 – 14.0mg/dl, Phenytoin 3.00 – 40.00umol/L, Sodium 75.0 – 250.0mmol/L, Uric Acid 0.50-17.00mg/dl Additionally a linearity was performed on the Vitros dHDL assay. Linearity was determined by diluting a concentrated high HDLC linearity fluid in saline, and samples were analyzed on the VITROS 5,1 FS system. The systems responses were plotted against the percent high pool and against calculated values to assess the degree to which the plotted curved conforms to a straight line. The equation of the line established was y=2.2744x-1.7229 with an R squared of 0.9985 this equation was used to plot regression concentrations. The data presented defines a linear range of the dHDL assay when run on the VITROS dHDL and established a reportable range of 2.66 to 135.64. This data supports a linearity claim of 3.0 – 100mg/dl.

e. *Analytical specificity:* Interferent studies were performed to determine the effect of levels of endogenous interferences on the performance of the VITROS Chemistry Products dHDL Reagent Pack using methods based on the NCCLS protocol EP7-P

f. Assay cut-off: Visual analysis determined the assay is linear across the range tested establishing a range and cutoff as listed for each marker assay. AST 3 – 750UL, CREATININE – 0.05 – 14.0mg/dl, Phenytoin 3.00 – 40.00umol/L, Sodium 75.0 – 250.0mmol/L, Uric Acid 0.50-17.00mg/dl and 3mg/dl and 100mg/dl for dHDL.

2. Comparison studies:

a. Method comparison with predicate device: The method comparison study used for the dHDL Cholesterol method followed NCCLS Guidelines EP9-A (Method Comparison and Bias Estimation Using Patient Samples).

b. Matrix comparison: A total of 107 human serum samples were assayed using the VITROS Chemistry products dHDL and the Bayer Direct HDL Cholesterol II assay. Single replicates of each sample were assayed on the Bayer ADVIA 1650 Chemistry System. The relationship between the two methods was determined by the least squares linear regression with patient samples form the VITROS dHDL as the "y" variable and those form the comparison device as the "x" variable. The relationship between the two assays determined by least square regression was VITROS dHDL Assay = 0.9472x X-0.0682 mg/dl with a correlation coefficient of 0.9836 where X equals the Bayer Direct HDL Cholesterol II assay.

3. Clinical studies:

a. Clinical sensitivity: N/A

b. Clinical specificity: N/A

4. Clinical cut-off: N/A

5. Expected values/Reference range: The expected values and the reference range of the VITROS dHDL cholesterol follow the guidelines of the CDC/NIH National Cholesterol Education Program (NCEP) Recommendations for Measurements of High Density Lipoprotein Cholesterol.

M. Instrument Name: VITROS 5,1 FS Chemistry System

N. System Descriptions:

1. Modes of Operation: random access, batch and STAT modes

2. Software: The VITROS 5,1 FS Chemistry System utilizes the QNX Neutrino v 6.1x or later operating system. It relies upon a touch screen or keyboard for user interface. Communications with external systems are run via Ethernet connection. Sample programming may be made from a Laboratory Information System to the analyzer via this connection.

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types: Yes ___X_____ or No _____

3. Sample Identification: Samples are identified via barcode or rack positioning.

4. Specimen Sampling and Handling: Samples consist of Plasma, serum, urine or cerebral spinal fluid depending upon analyte.

5. Assay Types: For the Vitro FS 5,1 Chemistry System – Chemistry Slides – Colorimetric, Poteniometric, Rate & Immunorate. MicroTip Reagents – Endpoint Colorimetric and Rate, Enzyme-coupled Immunoassay, Homogenous Turbidometric Immunoassay, Enhanced Latex ImmunoAssay

6. Reaction Types: For the Vitro FS 5,1 Chemistry System – Chemistry Slides – Colorimetric, Poteniometric, Rate & Immunorate. MicroTip Reagents – Endpoint Colorimetric and Rate, Enzyme-coupled Immunoassay, Homogenous Turbidometric Immunoassay, Enhanced Latex ImmunoAssay

7. Calibration: Calibrators are prepared from human serum and urine with specially prepared constituents added. Calibrators are placed upon the instrument, the VITROS 5,1 FS Chemistry system generates a worklist defining

which calibrator to use and where to place the calibrator. After the test is run, the system performs on-line calibration math via its internal processor and if successful (i.e. all pre-defined quality parameters stored in memory are met), an updated calibration curve is saved for each analyte calibrated.

8. Quality Control: Quality Control is managed via specially prepared human based sera and urine with specifically assayed values to establish an expected range of acceptable values.

O. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary.

P. Conclusion: I recommend that the Vitros Chemistry Products 5,1; Vitros Chemistry products dHDL; Vitros Chemistry products Calibrator kit 19 & Vitros Chemistry products FS Calibrator are substantially equivalent to their respective predicate devices.