510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k042006

B. Purpose for Submission:
New device

C. Analyte:
HDL Cholesterol

D. Type of Test:
Quantitative

E. Applicant:
Ortho-Clinical Diagnostics

F. Proprietary and Established Names:
VITROS® Chemistry Products dHDL Slides
VITROS® Products Calibrator Kit 25
VITROS®Products Performance Verifiers I and II

G. Regulatory Information:

1. Regulation section:
   862.1475, Lipoprotein Test System
   862.1150, Calibrator
   862.1660, Quality Control material (assayed and unassayed)

2. Classification:
   Class I that meets the limitations of exemptions 862.9 (c) (9)
   Class II
   Class I (reserved)

3. Product Code:
   LBS, JIS,JJY

4. Panel:
   75

H. Intended Use:

1. Intended use(s):
   See Indications for Use

2. Indication(s) for use:
   VITROS dHDL Slides are used to quantitatively measure HDL cholesterol (HDLC) concentration in serum and plasma. High Density Lipoprotein (HDL) cholesterol is used to evaluate the risk of developing coronary heart disease (CHD). The risk of CHD increases with lower HDL cholesterol concentrations.

   VITROS Chemistry Products Calibrator Kit 25 is used to calibrate VITROS Chemistry System for the quantitative measurement of HDL cholesterol using VITROS Chemistry Products dHDL Slides.

   VITROS Chemistry Products Performance Verifiers I and II are assayed controls used to monitor performance on VITROS Chemistry Systems.

3. Special condition for use statement(s):
   For in vitro diagnostic use only

4. Special instrument Requirements:
   VITROS Chemistry Systems

I. Device Description:

The VITROS Chemistry dHDL Slides, VITROS Chemistry Products Calibrator Kit 25 and VITROS Chemistry Products Performance Verifier I and II which are combined by the VITROS Chemistry System to perform the VITROS dHDL Slide assay

J. Substantial Equivalence Information:

1. Predicate device name(s):
   AHDL Flex reagent cartridge assay on the Dimension system

2. Predicate K number(s):
   k032798

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	Same	Same
Reportable range	5.0 – 110.0 mg/dL	0 -150 mg/dL
Sample type	Serum, heparin & EDTA plasma	Serum & Plasma

Differences		
Item	**Device**	**Predicate**
Sample size	10 µl	3 µl
Reagents	Dry chemistry	Liquid reagents
Test Type	Colorimetric endpoint	Bichromatic endpoint
Instrument	VITROS Chemistry System	Dade Dimension Clinical Chemistry system

K. Standard/Guidance Document Referenced (if applicable):

National Cholesterol Education Program (NCEP) guidelines "Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication No. 01-3670: May 2001
NCCLS EP5-A - Evaluation of Precision Performance of Clinical Chemistry Devices
NCCLS EP6-P – Evaluation of the Linearity of Quantitative Analytical Methods
NCCLS EP9-A – Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The VITROS dHDL Slide is a multilayered analytical element coated on a polyester support. The method is based on a HDL precipitation method followed by an enzymatic detection. A drop of sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. HDL is separated by the precipitation of non-High Density Lipoproteins (non-HDL) using phosphotungstic acid (PTA) and magnesium chloride ($MgCl_2$) in the spreading layer. The emulgent B-66 surfactant in the spreading layer aids in the selective dissociation of the cholesterol and cholesterol esters from the HDL lipoprotein complexes present in the sample. Hydrolysis of the HDL-derived cholesterol ester to cholesterol is catalyzed by a cholesterol ester hydrolase. Free cholesterol is then oxidized in the presence of cholesterol oxidase to form cholestenone and hydrogen peroxide. Finally, hydrogen peroxide oxidizes a leuco dye in the presence of peroxidase to generate a colored dye. The density of dye formed is proportional to the HDL cholesterol concentration present in the sample and is measured by reflectance spectrophotometry.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>
   a. *Precision/Reproducibility:*
      The evaluation followed NCCLS EP5-A, Evaluation of Precision Performance of Clinical Chemistry Devices. Two runs were performed on each of 22 different days on the VITROS 950 Chemistry System. Each run consisted of 3 control sera and 3 calibrator fluids assayed in duplicate. The order of the control sets in each run was randomized. Runs within day were separated by at least two hours. Three lots of VITROS dHDL Slides were

evaluated. The data was screened for gross outliers according to statistical outlier test in NCCLS EP5-A. No replicates were excluded from the analysis.

system	Conventional Units (mg/dL)					
	Mean Conc	Within-day SD	Within-Lab SD	Within-Lab CV%	No. Observations	No. Days
VITROS 950	37.6	0.7	1.0	2.7	88	22
	53.8	1.0	1.4	2.6	88	22
	99.2	2.1	2.5	2.5	88	22

system	SI Units (mmol/L)					
	Mean Conc	Within-day SD	Within-Lab SD	Within-Lab CV%	No. Observations	No. Days
VITROS 950	0.97	0.02	0.03	2.7	88	22
	1.39	0.03	0.04	2.6	88	22
	2.57	0.05	0.06	2.5	88	22

b. *Linearity/assay reportable range:*
Linearity studies were designed using NCCLS EP6-P, Evaluation of the Linearity of Quantitative Analytical Methods. A "high pool" was created by spiking commercially available purified human HDLC into a delipidized human serum pool to obtain a concentration of approximately 125 mg/dL HDLC. A delipidized human seum pool was used as the "low pool". The two pools were intermixed to obtain thirteen levels.

Six determinations of each of the 13 levels were made together with 6 determinations of each VITROS Chemistry Products Performance Verifiers I and II. The experiment was performed across three lots of VITROS Chemistry Products dHDL Slides. The HDLC results plotted against the percent high pool and against the calculated values to assess the degree to which the plotted curve conforms to a straight line. Analysis by linear regression indicated that the assay is linear across the range 0 to 114.6 mg/dL. The product claim for the reportable range is 5 to 110 mg/L.

c. *Traceability (controls, calibrators, or method):*
Values assigned to the VITROS Chemistry Products Calibrator Kit 25 for the VITRO Chemistry Products dHDL Slides are traceable to the CDC Lipid Standardization Program using the services of a CRMLN Network Laboratory.

d. Detection limit:
Lower Limit of Detection (LLD) is defined as the concentration that can be differentiated from zero using a predetermined confidence interval. The Lower Limit of Detection of the VITROS Chemistry Products dHDL Slides assay is typically no greater than 0.8 mg/dL (0.021 mmol/L).

e. Analytical specificity:
The substance listed in the package insert were tested with the VITRO Chemistry Products dHDL Slide at an HDLC concentration of approximately 40 mg/dL (1.03 mmmol/L) following NCCLS Protocol EP7 and found not to interfere, bias<3.8 mg/dL (<0.10 mmol/L), at the concentration shown in the package insert.

f. Assay cut-off:
Not applicable

2. Comparison studies:
   a. Method comparison with predicate device:
   Accuracy was evaluated based on NCCLS Protocol EP9-A2. The data below shows the results of a comparison of samples analyzed on the VITROS 950 Chemistry System with those analyzed on a method traceable to the CDC reference method and on a commercially available system.

				Conventional Units (g/dL)			SI Units (mmol/L)		
	n	slope	correlation coefficient	Conc.	Intercept	Sy.x	Conc.	Intercept	Sy.x
950 System vs Comparative method	134	1.00	0.996	11-104	0.09	1.63	0.28-2.69	0.00	0.04
950 System vs Commercial method	168	0.95	0.996	11-106	-0.64	1.78	0.28-2.74	-0.02	0.05

b. Matrix comparison:
Serum versus plasma studies were performed to demonstrate that samples types recommended are serum, heparin plasma and EDTA. Individual results from the determinations of each specimen were tabulated and reviewed for outliers as per NCCLS EP5-A. The bias values for matched patient samples collected in serum tubes, serum separator tubes, Li-heparin plasma tubes, Na-heparin plasma tubes, EDTA plasma tubes, and Li-heparin plasma separator tubes were within predetermined acceptance criteria. The bias values between serum samples and samples collected in fluoride/oxalate plasma tubes and citrate plasma tubes were outside of predetermined acceptance criteria for the VITROS dHDL Slides assay.

3. Clinical studies:
    a. *Clinical sensitivity:*
    Not applicable

    b. *Clinical specificity:*
    Not applicable

    c. *Other clinical supportive data (when a and b are not applicable)*

4. Clinical cut-off:
    Not applicable

5. Expected values/Reference range:

    The reference Interval for HDL is based on the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); Executive Summary. NIH Publication No. 01-3670, National Institutes of Health. Bethesda. Maryland: May 2001.

Cardiovascular Risk	Units
High	< 40 mg/dL
Low	≥ 60 mg/dL

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.