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

A. 510(k) Number:
k042521

B. Purpose for Submission:
New device

C. Analyte:
Apolipoprotein A1, Apolipoprotein B

D. Type of Test:
Quantitative

E. Applicant:
Ortho-Clinical Diagnostics, Inc.

F. Proprietary and Established Names:
Vitros Chemistry Products ApoA1 Reagent
Vitros Chemistry Products ApoB Reagent
Vitros Chemistry Products Calibrator Kit 21
Vitros Chemistry Products Calibrator Kit 22
Vitros Chemistry Products ApoA1 Performance Verifier 1
Vitros Chemistry Products ApoB Performance Verifier I

G. Regulatory Information:

1. Regulation section:
   862.1475, Lipoprotein Test System
   862.1150, Calibrator, Secondary
   862.1660, Single (specified) analyte controls (assayed and unassayed)

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

3. Product Code:
   JIT, MSJ, JJX

4. Panel:
   75

H. Intended Use:

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

2. Indication(s) for use:
   For *in vitro* diagnostic use only. VITROS Chemistry Products ApoA1 Reagent is used to quantitatively measure apolipoprotein A1 (ApoA1) concentration in human serum and plasma. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

   For *in vitro* diagnostic use only. VITROS Chemistry Products ApoB Reagent is used to quantitatively measure apolipoprotein B (ApoB) concentration in human serum and plasma. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

   For *in vitro* diagnostic use only. VITROS Chemistry Products Calibrator Kit 21 is used to calibrate VITROS 5,1 FS Chemistry Systems for the quantitative measurement of apolipoprotein A1 (ApoA1).

   For *in vitro* diagnostic use only. VITROS Chemistry Products Calibrator Kit 22 is used to calibrate VITROS 5,1 FS Chemistry Systems for the quantitative measurement of apolipoprotein B (ApoB).

   For *in vitro* diagnostic use only. VITROS Chemistry Products ApoA1 Performance Verifier I is an assayed control used to monitor the performance of ApoA1 Reagent on VITROS 5,1 FS Chemistry Systems.

   For *in vitro* diagnostic use only. VITROS Chemistry Products ApoB Performance Verifier I is an assayed control used to monitor the performance of ApoB Reagent on VITROS 5,1 FS Chemistry System.

3. Special condition for use statement(s):
   Prescription Use only
4. Special instrument Requirements:
   VITROS 5,1 FS Chemistry System

I. Device Description:

The VITROS ApoA1 and ApoB Reagents are dual chambered packages containing stable, ready-to-use liquid reagents that are used in two-step reactions to quantitatively measure ApoA1 and ApoB. VITROS Chemistry Products Calibrator Kit 21 and 22 are prepared from processed human serum to which organic salts, buffers, organic compounds, bovine serum albumin, and preservatives have been added. The ApoA1 and ApoB Performance Verifiers are prepared from processed human serum to which organic salts, buffers, organic compounds, bovine serum albumin, and preservatives have been added.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dade Behring N Antisera to Human Apolipoprotein A1 and Apolipoprotein B Reagent and N Apolipoprotein Standard Serum

2. Predicate K number(s):
   k860894, k041870

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Basic principle	Immunoturbidimetric assay	Same
Intended use	Quantitative measurement of ApoA1 and ApoB	Same
Differences		
Item	**Device**	**Predicate**
Sample type	Serum and heparin plasma	Serum
Instrumentation	VITROS 5,1 FS Chemistry System	Dade BN ProSpec
Reportable range:		
ApoA1	30-240 mg/dL	19-600 mg/dL
ApoB	35-300 mg/dL	25-400 mg/dL
Reactive ingredients:		
ApoA1	Goat antisera to human Apo A1	Rabbit antisera to human Apo-A1
ApoB	Goat antisera to human Apo B	Rabbit antisera to human ApoB
Performance verifiers:		
Matrix	Processed human serum to which inorganic salts, buffers, organic compounds, bovine serum albumin and preservatives have been added	Stabilized reagent from human origin
Form	Liquid	Lyophilized

K. Standard/Guidance Document Referenced (if applicable):
NCCLS EP5-A, NCCLS EP6-A, NCCLS EP7-A, NCCLS EP9-A2, NCCLS C28

L. Test Principle:
The VITROS ApoA1 and ApoB Reagents are dual chambered packages containing stable, ready-to-use liquid reagents that are used in a two-step reaction. Samples,

calibrators and controls are automatically diluted in saline containing surfactant and mixed with Reagent 1 containing a polymer and surfactant. Addition of antisera specific for human ApoA1 (Reagent 2 - ApoA1 reagents) and for ApoB (Reagent 2 - ApoB Reagents) produces an immunochemical reaction yielding antigen/antibody complexes. The light scattering properties of the antigen/antibody complexes increases increase solution turbidity proportional to ApoA1 and ApoB concentrations in the sample. The turbidity is measured spectrophotometrically at 340 nm. Once a calibration has been performed for each reagent lot, the concentration in each unknown sample can be determined using the stored calibration curve and the measured absorbance obtained in the assay of the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Quality control materials were analyzed following NCCLS EP5. Within day precision was determined using two runs per day with two replications per run. Within lab precision was determined using a single lot of reagents and four calibrations.

VITROS ApoA1 Precision

Mean Conc.	Within day SD	Within Lab SD	Within-Lab CV%	No. Days	No. Observations
88.55	0.850	1.573	1.8	22	88
124.78	1.469	2.704	2.2	22	88
176.03	3.586	6.088	3.5	22	87

VITROS ApoB Precision

Mean Conc.	Within day SD	Within Lab SD	Within-Lab CV%	No. Days	No. Observations
57.53	0.000	2.151	3.7	22	87
117.82	2.361	3.696	3.1	22	88
134.62	2.451	5.288	3.9	22	88

b. Linearity/assay reportable range:

The evaluations of the linearities of ApoA1 and ApoB were performed based on NCCLS EP6-A. The high pool was the high level calibrator with a concentration of 243 mg/dL for ApoA1 and 301 mg/dL for ApoB. The low pool was the low level calibrator with a concentration of 28 mg/dL for ApoA1 and 0 mg/dL for ApoB. Add-mixtures of the high and low pool created 13 levels for ApoA1 and 11 levels for ApoB spanning the assay reportable range. Three determinations of each of the evaluation fluids were made, together with 3 determinations of VITROS Chemistry Products Performance Verifiers I, ApoB Performance Verifier and BioRad Liquichek Control level 3. The results showed that the biases between

predicted and calculated results were acceptable for all linearity fluids tested. In addition, recovery studies were performed by diluting five patient samples, one high calibrator, and one concentrated patient pool 1:2 with Apo Diluent and measuring ApoA1 and ApoB using two different lot numbers of reagent. The average mean percent recovery value across the reagent lots was 101.7 % for ApoA1 and 103.0 % for ApoB with an individual sample recovery range of 91.3 % to 108.2 % for ApoA1 and 95.0% to 108.8% for ApoB. The dilution of patient samples with Apo diluent was determined to be acceptable up to a 1:2 dilution.

c. *Traceability (controls, calibrators, or method):*
Values assigned to the VITROS Chemistry Products Calibrator Kit 21 for the ApoA1 assay are traceable to WHO/IFCC SP1-01 Reference Material. Values assigned to the VITROS Chemistry Products Calibrator Kit 22 for the ApoB assay are traceable to WHO/IFCC SP3-08.

Real time stability studies were conducted to establish expiration dates. The calibrator and performance verifiers are stable until the date specified in the labeling for opened and un-opened vials.

d. *Detection limit:*
The Lower Limit of Detection (LLD) is defined as the concentration that can be distinguished from zero using a predetermined confidence interval. The pre-determined confidence interval for the lower limit of detection was calculated by multiplying 3.3 times the square root of the squares of the calibration error standard deviation plus the pooled replicate standard deviation. Calibration error at the mean response level of the low analyte fluid was estimated by Monte Carlo simulation using six replicates per calibrator level. This equation is equivalent to approximately a 99.9% confidence interval from zero for the lower limit of detection. The Lower Limit of Detection of the VITROS Chemistry Products ApoA1 Reagent assay is 2.9 mg/dL. The Lower Limit of Detection of the VITROS Chemistry Products ApoB Reagent assay is 4 mg/dL.

e. *Analytical specificity:*
The effect of triglyceride concentration on the VITROS Chemistry Products ApoA1 and ApoB assays was assessed by plotting the percent bias observed between the mean result obtained with the VITROS method and the predicate method. Triglyceride bias was acceptable up to 1000 mg/dL. The limits for acceptable triglyceride bias were calculated based on the average level of ApoA1 or ApoB present in the patient samples analyzed. For ApoA1 the limit was +/- 18 mg/dL. For ApoB, the limit was +/- 12 mg/dL. Bilirubin at a

concentration of 60 mg/dL, Intralipid at 1000 mg/dL, ascorbic acid at 3 mg/dL, and hemoglobin at 1000mg/dL did not interfere with the ApoA1 and ApoB assays. Several other substances were tested and found not to interfere. A list of these substances is found 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 show the results of a comparison of samples analyzed on the VITROS 5,1 FS Chemistry System with those analyzed on the Dade Behring BN ProSpec Nephelometer commercially available system.

Method Comparison for dLDL: Serum

5,1 FS System vs. Dade Behring BN ProSpec	n	Slope	Correlation Coefficient	Conventional Units (mg/dL) Range of Sample Conc.	Intercept	Sy.x	SI Units (mmol/L) Range of Sample Conc.	Intercept	Sy.x
ApoA1	136	0.98	0.987	49.10–237.66	-3.81	6.12	1.06–7.76	-0.099	0.16
ApoB	137	1.00	0.985	39.96-225.07	-3.88	4.54	0.37-2.25	-0.04	0.045

   b. Matrix comparison:
   Sample types recommended are serum and heparin plasma. Sixty matched serum and Li-heparin plasma patient samples were tested. The bias between the mean value for each serum and plasma sample was calculated. Bias values were plotted and fell within predetermined acceptance limits.

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 evaluation was performed according to NCCLS C28A. A total of 121 apparently healthy subjects were tested with two lots of reagents. The 2.5 and 97.5 percentile values of the distribution and their 90 percent confidence intervals were calculated for each lot. The final reference interval was calculated as the average of the reference intervals of the two lots and is the central 95^{th} percentile of results. The reference interval for ApoA1 is 101-215 mg/dL and for ApoB is 51-132 mg/dL.

N. Conclusion:

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