

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k063608

B. Purpose for Submission:

New device
New calibrator
New control

C. Measurand:

Apolipoprotein A-I (APOAI)
Apolipoprotein B (APO B)

D. Type of Test:

Quantitative immunoassay, nephelometric

E. Applicant:

Dade Behring Inc.

F. Proprietary and Established Names:

Dimension Vista™ APOAI Flex® reagent cartridge
Dimension Vista™ APOB Flex® reagent cartridge
Dimension Vista™ Apolipoprotein calibrator (APO CAL)
Dimension Vista™ Apolipoprotein control (APO CON)

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1475, Lipoprotein test system
21 CFR 862.1150, Calibrator
21 CFR 862.1660, Quality control material (assayed and unassayed)

2. Classification:

Respectively:

Class I, meets the limitations to the exemption 21 CFR 862.9(c)(4)
Class II
Class I, reserved

3. Product code:

MSJ, JIT, JJY

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use.

2. Indication(s) for use:

Dimension Vista APOAI Flex reagent cartridge :

The method is an in vitro diagnostic test for the quantitative determination of apolipoprotein A-I in human serum, heparinized plasma, or EDTA plasma on the Dimension Vista system. Measurements of apolipoprotein A-I aid in the diagnosis and treatment of lipid disorders, various liver and renal diseases, and in the assessment of risk for atherosclerosis and cardiovascular disease.

Dimension Vista APOB Flex reagent cartridge :

The method is an in vitro diagnostic test for the quantitative determination of apolipoprotein B in human serum, heparinized plasma, or EDTA plasma on the Dimension Vista system. Measurements of apolipoprotein B aid in the diagnosis and treatment of lipid disorders, various liver and renal diseases, and in the assessment of risk for atherosclerosis and cardiovascular disease.

Dimension Vista Apolipoprotein Calibrator:

Apolipoprotein Calibrator is an in vitro diagnostic product for the calibration of apolipoprotein A-I (APOAI) and apolipoprotein B (APOB) on the Dimension Vista system.

Dimension Vista Apolipoprotein Control:

Apolipoprotein Control is an in vitro diagnostic product for the assessment of precision and analytical bias of apolipoprotein A-I (APOAI) and apolipoprotein B (APOB) on the Dimension Vista system.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

Dade Behring Dimension Vista system

I. Device Description:

The Dimension Vista APOAI Flex and APOB Flex reagent cartridges each consist of 12 reagent wells. Wells 1-4 contain either APOAI or APOB supplement reagent. Wells 11 and 12 contain rabbit antiserum specific to either apolipoprotein A-I or apolipoprotein B. The remaining wells 5-10 are used for patient sample dilution and mixing.

The Dimension Vista Apolipoprotein calibrator is a lyophilized, human serum based product containing apolipoprotein A-I and apolipoprotein B. It is packaged in 4 vials. Before use, the contents should be reconstituted with 1.0 mL of distilled water. The

analyzer automatically dilutes the calibrator with System Diluent to achieve concentrations spanning the assay range.

The Dimension Vista Apolipoprotein control is a lyophilized, human serum based product containing apolipoprotein A-I and apolipoprotein B. It is packaged in 4 vials. Before use, the contents should be reconstituted with 1.0 mL of distilled water.

The sponsor indicates that human source materials were tested and found to be negative for Human immunodeficiency virus (HIV) 1 and 2, Hepatitis B virus (HBV) and Hepatitis C virus (HCV). The tests were either FDA approved methods or methods found to be in conformance with the IVD Directive in the European Union.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Antisera to Human Apolipoprotein A-I and Apolipoprotein B
Dade Behring N Apolipoprotein Standard Serum
Dade Behring Apolipoprotein Control Serum CHD
2. Predicate 510(k) number(s):
k860894, k041870, k993310
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
<u>Dimension Vista APOAI and APO B Flex Reagent Cartridges:</u>		
Assay method	Nephelometric immunoassay	Nephelometric immunoassay
Assay antibody	Rabbit	Rabbit
<u>Dimension Vista APO CAL and APO CON:</u>		
Calibrator composition	Lyophilized human serum containing apolipoprotein A-1 and apolipoprotein B	Lyophilized human serum containing apolipoprotein A-1 and apolipoprotein B

Similarities		
Item	Device	Predicate
Control composition	Lyophilized human serum containing apolipoprotein A-I and apolipoprotein B	Lyophilized human serum containing apolipoprotein A-I and apolipoprotein B

Differences		
Item	Device	Predicate
<u>Dimension Vista APOAI and APO B Flex Reagent Cartridges:</u>		
Test System	Dimension Vista	BN systems
Sample type	Serum, lithium or sodium heparin plasma, EDTA plasma	Serum only
Reportable Range APOAI	19-600 mg/dL	Not specified, dependent on protein concentration of standard
APO B	26-400 mg/dL	Not specified, dependent on protein concentration of standard
<u>Dimension Vista APO CAL:</u>		
Traceability APOAI Traceability APOB	BCR-393 IRP SP3-07	IRP SP1-01 IRP SP3-07

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

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition (CLSI EP5-A)
- Interference Testing in Clinical Chemistry; Approved Guideline (CLSI EP7-A2)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline Second Edition (CLSI EP9-A2)

L. Test Principle:

Apolipoprotein A-I and apolipoprotein B in the serum or plasma sample form immune complexes in an immunochemical reaction with protein specific antibodies. These complexes scatter a beam of light as it passes through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

M. Performance Characteristics (if/when applicable):**1. Analytical performance:****a. *Precision/Reproducibility:***

The precision study was performed over a period of 20 days following the protocol outlined in CLSI EP5-A2.

For the APOAI assay, sample material included the Dade Behring Vista Apolipoprotein control (168 mg/dL), two serum pools (48 and 508 mg/dL) and two lithium heparin plasma pools (103 and 227 mg/dL). Repeatability ranged from 2.0-4.4% CV and within lab imprecision ranged from 2.8-4.9% CV.

For the APOB assay, sample material included the Dade Behring Vista Apolipoprotein control (96 mg/dL), three serum pools (43, 52, and 370 mg/dL) and two lithium heparin plasma pools (98 and 146 mg/dL). Repeatability ranged from 1.4-6.4% CV and within lab imprecision ranged from 2.6-7.2% CV.

b. *Linearity/assay reportable range:*

The reportable range of the APOAI assay is 19-600 mg/dL.

The reportable range of the APOB assay is 26-400 mg/dL.

Linearity was evaluated by comparing the observed versus expected values obtained with the Dimension Vista APOAI and APO B methods. Natural serum samples with high concentration of APOAI and APOB were mixed with System Diluent in twelve (12) different proportions across the range of the assay. For the APOAI method, when observed results were compared to expected results, recovery ranged from 92-111%. For the APOB method, recovery ranged from 95-103%.

High dose hook effect was evaluated by testing sera with elevated APOAI or APOB. No hook effect was observed with samples up 829 mg/dL and 967 mg/dL respectively.

Samples above assay range are reported by the analyzer as >600 mg/dL (APOAI) or >400 mg/dL (APOB). These samples are automatically diluted

1:100 with System Diluent on board the analyzer.

Samples below the assay range are reported as <19 mg/dL (APOAI) or <26 mg/dL (APOB).

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Calibrators and controls are required with this assay and are specifically identified in the labeling. They are both provided separately, and are obtaining clearance with this submission. See the device description section, above.

Traceability and Value Assignment:

Dimension Vista Apolipoprotein Calibrator (APO CAL) and Apolipoprotein Control (APO CON) are traceable to protein reference material BCR-393 (APOAI) and IRP SP3-07 (APOB).

The value assignment process is as follows. Master Calibrators are prepared internally and values are assigned from protein reference materials BCR-393 and IRP SP3-07. The Master Calibrators are tested with along with the new lot of APO CAL or APO CON on multiple analyzers and multiple assay runs.

Stability:

The real time and accelerated stability study protocols were reviewed for APO CAL and APO CON and found to be acceptable.

- d. *Detection limit:*

The sponsor's labeling states the lower limit of the reportable range to be 19 mg/dL (APOAI) and 26 mg/dL (APOB) which were previously established in k860894 and validated for use on the Vista. In addition, limit of blank studies were performed and the results were well below the lower limit stated.

- e. *Analytical specificity:*

Interference testing was performed according to CLSI EP7-A2, to determine the effect of various endogenous and exogenous substances on the assay. Hemoglobin hemolysate (up to 1000 mg/dL), conjugated and unconjugated bilirubin (up to 60 mg/dL), and a panel of commonly ingested substances, over-the-counter drugs and prescription drugs did not interfere with the assay. A list of these substances can be found in the package insert. The sponsor defined interference as a difference in recovery between the test sample and control sample greater than 10%.

The effect of rheumatoid factor (RF) was evaluated by testing mixtures of serum samples with known elevated RF and samples with low RF. The APOAI and APOB concentrations were determined for each sample in replicates of five on the Dimension Vista System. For each sample preparation, the percent recovery was calculated by comparing the measured

result to the expected result. The sponsor defined interference as a difference in recovery between the actual and expected values of greater than 10%. Levels of RF up to 1400 IU/mL did not interfere.

The effect of interference by elevated total protein was determined by testing the total protein and APOAI and APOB concentrations in a neat sample. The neat sample was then spiked with additional protein. For each sample preparation, the percent recovery was calculated by comparing the measured result to the initial result. The sponsor defined interference as a difference in recovery between the actual and initial values of greater than 10%. Levels of total protein up to 13.8 g/dL did not interfere.

The sponsor states in the labeling under “Limitations of Procedure” that the effect of elevated triglycerides and chylomicrons was not evaluated.

- f. Assay cut-off:*
Not applicable

2. Comparison studies:

- a. Method comparison with predicate device:*

Serum samples were tested in singleton on the Dimension Vista APOAI and APOB methods and the Dade Behring BN ProSpec test system. The method used to fit the linear regression line was Passing Bablok.

Comparative Method	n	Slope	Intercept	Correlation Coefficient
APOAI	72	1.007	-0.038	0.997
APOB	77	1.011	-0.004	0.995

- b. Matrix comparison:*

The sponsor demonstrated equivalence between serum and EDTA, lithium heparin, and sodium heparin plasmas by conducting the following study. Ten matched serum and plasma sets with APOAI and APOB values spanning the assay range were tested on the Dimension Vista APOAI and APOB methods and the results compared. All plasma samples tested recovered within $\pm 5\%$ of its matched serum sample.

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):
Not applicable.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Expected values are based on literature.

Apo AI	women	125 – 215 mg/dL [1.25 - 2.15 g/L]
	men	110 – 205 mg/dL [1.10 - 2.05 g/L]
Apo B	women	55 – 125 mg/dL [0.55 - 1.25 g/L]
	men	55 – 140 mg/dL [0.55 - 1.40 g/L]
Apo B/Apo A-I	women	0.30 - 0.90
	men	0.35 - 1.00

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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