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

A. 510(k) Number:
k073072

B. Purpose for Submission:
New Submission

C. Measurand:
high-density lipoprotein cholesterol (HDL Cholesterol)

D. Type of Test:
Quantitative colorimetric

E. Applicant:
Dade Behring, Inc.

F. Proprietary and Established Names:
Dimension AHDL Flex Reagent Cartridge

G. Regulatory Information:

1. Regulation section:
   21CFR Sec. 862.1475-Lipoprotein test system.
2. Classification:
   Class I, meets the limits to exemption under 862.9 (c) (4)
3. Product code:
   JHM - Colorimetric Method, Lipoproteins
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See Indication(s) for use below
2. Indication(s) for use:
   The AHDL method is an in vitro diagnostic test for the quantitative measurement of high-density lipoprotein cholesterol (HDL-C) in human serum and plasma on the Dimension® clinical chemistry system. Measurements of HDL-C are used as an aid in the diagnosis of lipid disorders (such as diabetes mellitus), various liver and renal diseases and in the assessment of risk for atherosclerosis and cardiovascular disease.
3. Special conditions for use statement(s):
   For prescription use.
4. Special instrument requirements:
   Dimension® clinical chemistry system

I. Device Description:

Reagents

Wells	Form	Ingredient	Concentration	Source
1,2,3	Liquid	HEPES Buffer	10.07 mmol/L, pH 7.4	
Reagent 1		2-(N-cyclohexylamino)-ethanesulfonic acid	96.95 mmol/L	

		Dextran Sulfate	1.5 g/L	
		Magnesium Nitrate Hexahydrate	≥11.7 mmol/L	
		N-(2-hydroxy-3-sulfopropyl)-3, 5-dimethoxyaniline	0.96 mmol/L	
		Ascorbate Oxidase	≥50 µkat/L	bacterial
		Peroxidase	≥ 16.7 µkat/L	horseradish
		Preservative		
4	Liquid	HEPES Buffer	10.07 mmol/L, pH 7.0	
Reagent 2		PEG-Cholesterol Esterase	≥ 3.33 µkat/L	bacterial
		PEG-Cholesterol Oxidase	≥ 127 µkat/L	bacterial
		Peroxidase	≥ 333 µkat/L	horseradish
		4-Amino-Antipyrine	2.46 mmol/L	
		Preservative		
5,6	Liquid	NaOH	1.00 M	

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dimension® AHDL Flex® reagent cartridge
2. Predicate 510(k) number(s):
   k032798
3. Comparison with predicate:

Item	Device	Predicate
Intended Use	The AHDL method is an *in vitro* diagnostic test for the quantitative measurement of high-density lipoprotein cholesterol (HDL-C) in human serum and plasma on the Dimension® clinical chemistry system. Measurements of HDL-C are used as an aid in the diagnosis of lipid disorders (such as diabetes mellitus), various liver and renal diseases and in the assessment of risk for atherosclerosis and cardiovascular disease.	The AHDL method for the Dimension® clinical chemistry system is an *in vitro* diagnostic test intended to quantitatively measure high-density lipoprotein cholesterol (HDL-C) in human serum and plasma. HDL-C measurements are used as an aid in the diagnosis of lipid disorders
Sample Type	Human Serum or Plasma	Human Serum or Plasma
Sample Size	3 uL	3 uL
Measurement method	PEG HDL-C (polyethylene modified)	Accelerator Selective Detergent Methodology
Measuring Range	3-150 mg/dL	3-150 mg/dL

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

- "Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff "- 4/25/2006

- CLSI - Method Comparison and Bias Estimation Using Patient Samples - EP09-A2
- CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2
- CLSI - Interference Testing in Clinical Chemistry - EP07-A2
- CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation - EP17-A
- Cholesterol Reference Method Laboratory Network (CRMLN) Certification

L. Test Principle:

The AHDL assay measures HDL cholesterol levels directly without the need for sample pretreatment or specialized centrifugation steps, using a two reagent format. In the first reaction, chylomicrons, VLDL and LDL form water soluble complexes with dextran sulfate in the presence of magnesium sulfate. These complexes are resistant to the polyethylene glycol (PEG)-modified cholesterol esterase and cholesterol oxidase that react with HDL cholesterol. In the presence of oxygen, the HDL cholesterol is oxidized to Δ4-cholestenone and hydrogen peroxide. The generated hydrogen peroxide then reacts with 4-aminoantipyrine and sodium N-(2-hydroxy-3-sulfopropyl)-3,5-dimethoxyaniline (HSDA) in the presence of peroxidase to form a colored dye that is measured using a bichromatic (600/700 nm) endpoint technique. The color intensity of the dye is directly proportional to the serum HDL-C concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

		Repeatability		With-in Lab	
Sample	**Mean (mg/dL)**	**SD (mg/dL)**	**%CV**	**SD (mg/dL)**	**%CV**
Bio-Rad Liquid Unassayed Multiqual					
Level 1	25	0.6	2.3	0.6	2.4
Level 2	44	0.6	1.4	0.7	1.7
Level 3	58	1.2	2.2	1.3	2.2
Serum Pools					
Level 1	48	0.9	1.9	1.0	2.1
Level 2	92	1.3	1.4	1.7	1.8

The reproducibility testing was conducted in accordance with the CLSI/NCCLS Approved Guideline for User Evaluation of Precision Performance of Clinical Chemistry Devices EP5-A2. For each test level, a

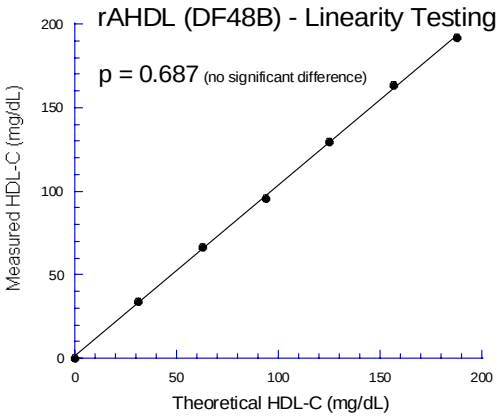
single test from two independent cups was analyzed twice per day.

b. *Linearity/assay reportable range:*

The Dimension AHDL method demonstrated visual and statistical linearity across the claimed assay range of 3 to 150 mg/dL. The Dimension AHDL method is linear up to and above the level 3 calibrator (>150 mg/dL).

Linearity was evaluated by comparing observed versus expected values obtained with the Dimension® AHDL method using a series of samples. The samples were prepared by taking the high level calibrator diluted across the expected range with the zero level calibrator.

Theoretical HDL-C (mg/dL)	**Measured HDL-C** (mg/dL)	**Percent Recovery**
0.00	0.88	N/A
5.65	5.53	97.96
11.31	10.93	96.68
22.61	21.91	96.92
45.22	47.02	103.97
90.44	92.70	102.50
135.65	135.56	99.94
180.87	180.87	100.00



x = 1.024 y + 1.113
r = 1.00

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* This method has been evaluated by and met the certification acceptance criteria of the Cholesterol Reference Method Laboratory Network (CRMLN).

The calibrator was cleared under k983850

Controls are not part of this submission nor does the applicant recommend any particular commercially available quality control material.

d. Detection limit:

Limit of Detection: 3 mg/dL

The limit of detection represents the lowest concentration of high density lipoprotein cholesterol that can be detected with at least 95% probability. CLSI/NCCLS EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation, was followed using 60 replicate determinations at two concentration levels to determine the Limit of Detection.

e. Analytical specificity:
The AHDL method was evaluated for interference according to CLSI EP7-A2.
Bias was defined as the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% was considered interference.

Substance Tested	**Substance Concentration**	**HDL Cholesterol mg/dL**	**Bias %**
Hemoglobin (hemolysate)	Hemoglobin (monomer) 1000 mg/dL	37	< 10%
Bilirubin (unconjugated)	80 mg/dL	43	< 10%
Bilirubin (conjugated)	60 mg/dL	43	< 10%
Intralipid	1000 mg/dL	37	< 10%

f. Assay cut-off:
Not Applicable

2. Comparison studies:
a. Method comparison with predicate device:

Method comparison testing was conducted following CLSI Approved Guideline for Method Comparison and Bias Estimation Using Patient Samples; EP9-A2. A total of 134 serum samples were analyzed in parallel for new AHDL and current AHDL on a Dimension ® clinical chemistry analyzer. Seven of the 134 samples were prepared by adding concentrated high density lipoprotein from human serum into normal human serum.

Data were analyzed by least squares linear regression analysis. A subset of the samples with HDL-C concentrations < 60 mg/dL was also analyzed separately.

Slope	Intercept (mg/dL)	r	Sy,x	n	Sample Range (mg/dL)
1.04 ± 0.01	-3.9 ± 0.5	1.00	2.77	130	4 – 131
0.99 ± 0.02	-2.5 ± 0.8	0.98	2.53	98	4 – 59

b. Matrix comparison:

Comparison of sixty nine matched serum and lithium heparin plasma samples on the Dimension® system and sixty nine matched serum and sodium heparin plasma samples gave the following linear regression statistics:

Serum Vs.	Slope	Intercept mg/dL	Correlation Coefficient	n
Lithium Heparin	1.00	0.74	1.00	69
Sodium Heparin	1.01	0.40	1.00	69

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:
   The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) provides the following classifications of HDL-C concentrations:

   HDL < 40 mg/dL - Low HDL Cholesterol
   HDL ≥ 60 mg/dL - High HDL Cholesterol

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.