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

A. 510(k) Number:

k071706

B. Purpose for Submission:

New Device

C. Measurand:

HDL Cholesterol assay and calibrator

D. Type of Test:

Quantitative colorimetric test and calibrator

E. Applicant:

Clinical Data, Inc.

F. Proprietary and Established Names:

Envoy 500 HDL Cholesterol Reagent Kit

G. Regulatory Information:

1. Regulation section:

   CFR 21 section 862.1475 - Lipoprotein test system

   CFR 21 section 862.1150 - Calibrator

2. Classification:

   Assay - Class I, subject to limitation to exemption 21 CFR 862.9(c)(4)

   Calibrator - Class II

3. Product code:

   LBS, JIT

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Envoy® 500 HDL Cholesterol Reagent and Envoy® 500 HDL Calibrator are intended for use with the Envoy® 500 Chemistry System as a system for the quantitative determination of high density lipoprotein (HDL) cholesterol in serum and plasma. HDL cholesterol measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases, and for the assessment of the risk of developing cardiovascular disease.

   This reagent is intended to be used by trained personnel in a professional setting and is not intended for home use.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Envoy 500 Chemistry System

I. Device Description:

The Envoy® 500 HDL Cholesterol Reagent is a two-part reagent that is calibrated with the Envoy® 500 HDL Calibrator for use with the Envoy® 500 Chemistry System. The reagents consist of 27 mL boats of Envoy 500 HDL Cholesterol Reagent 1 and 9 ml bottles of reagent 2. Reagent 1 contains < 1,000 U/L cholesterol oxidase (E. coli), < 1,300 ppg U/L peroxidase (horseradish), < 1 mmol/L disodium N,N-bis(4-sulfobutyl)-m-toluidine, < 1 mmol/L accelerator, < 0.06% preservative, buffer, and other ingredients. HDL Cholesterol Reagent 2 contains < 1,500 U/L cholesterol esterase (Pseudomonas sp.), < 1 mmol/L 4-aminoantipyrine, < 2% detergent, < 0.15% restrainer, < 3,000 U/L ascorbate oxidase (Curcubita), < 0.06% preservative, buffer, and other ingredients. The calibrator contains a lyophilized human serum preparation of the various classes of lipoprotein including high density lipoproteins.The source materials in this product have been tested and found to be

non-reactive for HBsAg and antibodies to HIV-1, HCV-2, and Hepatitis C Virus (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Genzyme Ultra N-geneous HDL Cholesterol Reagent and Genzyme Ultra N-geneous HDL Cholesterol Calibrator

2. Predicate K number(s):

   k021316

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Quantitative determination of HDL cholesterol in serum and plasma	Same
Analyte	HDL	Same
Calibrator	Lyophilized Human Serum	Same
Assay principle	Quantitative colorimetric	Same

Differences		
Item	Device	Predicate
Reportable Range	5 to 150 mg/dL	2.5 to 200 mg/dL

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

CLSI EP-17A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI EP-3T: Tentative Guidelines for Manufacturers for Establishing Performance Claims for Clinical Chemical Methods, Replication Experiment

L. Test Principle:

This assay determines high density lipoprotein cholesterol through the accelerator selective detergent methodology. This procedure measures HDL-cholesterol in a two step reaction sequence. In the first step, non-HDL cholesterol is rendered non-reactive. In the second step, HDL cholesterol is solubilized using a selective detergent and reacts to produce a red chromogen. This method is based on accelerating the reaction of cholesterol oxidase (CO) with non-HDL unesterified cholesterol and dissolving HDL cholesterol selectively using a specific detergent. In the first reagent, non-HDL

unesterified cholesterol is subject to an enzyme reaction and the peroxide generated is consumed by a peroxidase reaction with DSBmT yielding a colorless product. The second reagent consists of a detergent (capable of solubilizing HDL cholesterol), cholesterol esterase (CE), and chromagenic coupler to develop color for the quantitative determination of HDL cholesterol.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. *Precision/Reproducibility:*

   Estimates of imprecision were determined through the replicate analysis of two serum controls. The controls were assayed in triplicates in two independently calibrated runs separated by at least three hours. The daily protocol was repeated for a total of eight days using five Envoy 500 HDL Cholesterol Reagent boats on a single Envoy 500 Analyzer. Average results for the two controls were reported for every run. Estimates of within run and total imprecision were calculated and are shown below. The level 1 results from one of the runs were removed from the calculations.

			Within Run		Total	
Sample	n	mean	1SD	%CV	1SD	%CV
Level 1	45	36.8	0.52	1.4%	0.72	2.0%
Level 2	48	71.1	0.68	1.0%	1.25	1.8%

   b. *Linearity/assay reportable range:*

   Linearity was evaluated by testing 12 samples with equally spaced HDL concentrations ranging from 0 to over 170 mg/dL. The samples were prepared by diluting a 3300 mg/dL human HDL Cholesterol concentrate with analyte stripped serum. The standards were then analyzed on the ENVOY 500 analyzer across 4 independently calibrated runs and compared to their dilution factors by least squares linear regression. The assay is linear across the reportable range of 5 mg/dL to 150 mg/dL HDL cholesterol as shown by mean regression residuals that are less than 1 mg/dL for all pools that describe this range and a correlation coefficient of 0.9998.

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

   Stability testing was performed by the manufacturer. The calibrators and reagents are stable until the expiration date on the label when stored as instructed.

On board stability was performed on the Envoy 500 analyzer demonstrated that the calibrators and reagents are stable for 14 days when stored on board the Envoy 500 analyzer.

Calibrator set points are assigned by the calibrator manufacturer and are traceable to the CDC described reference method for the determination of HDL cholesterol. These calibrators are not traceable to the Cholesterol Reference Method Laboratory Network for HDL cholesterol results produced using the Envoy 500 instrument application.

d. *Detection limit:*

A limit of quantitation (LoQ) study was conducted based on procedures described in CLSI EP17-A. The limit of the blank (LoB) of 0.29 mg/dL and limit of detection (LoD) of 0.46 mg/dL were calculated as described in the CLSI document. The LoQ of 0.46 mg/dL was determined to be equal to the LoD and was calculated assuming a zero method bias and an acceptable error of 2 mg/dL. The LoQ is lower than the lower limit of usable range which is set at 5 mg/dL.

e. *Analytical specificity:*

The effects of potential interfering substances were tested by assaying spiked serum pools. A serum pool with an HDL concentration of approximately 55 mg/dL was prepared from individual patient specimens and divided into aliquots. All but one of the aliquots were spiked with interferants at the concentrations shown below. The unspiked and spiked pools were tested multiple times in a single analytical run on the Envoy 500. Substances that affect results by more than 3 mg/dL compared to the interferant free sample were reported as interfering substances in the package insert.

Interfering Substance	Levels Tested
Ascorbic Acid	0, 0.75, 1.5, 2.25, 3.0 mg/dL
Ditaurobilirubin	0, 8, 16, 24, 32, 40 mg/dL
RBC hemolysate	0, 40, 80, 120, 160, 200 mg/dL
Intralipid, 20% solution	0, 80, 160, 240, 320, 400 mg/dL 0, 400, 800, 1200, 1600, 2000 mg/dL

The ascorbic acid, ditaurobilirubin, and RBC hemolysate spiked samples all had a bias of less than 3 mg/dL compared to the unspiked sample. The results of triglyceride interference (performed with intralipid) resulted in the bias shown below.

Changes in

Triglyceride Concentration	Recoveries
240 mg/dL	-3.3 at 52 mg/dL
400 mg/dL	-5.4 at 52 mg/dL
800 mg/dL	-1.5 at 54 mg/dL
2000 mg/dL	+2.5 at 54 mg/dL

   f. *Assay cut-off:*

   Not applicable

2. Comparison studies:

   a. *Method comparison with predicate device:*

   One hundred sixty serum and 152 plasma specimens were collected from
   individual adult patients. Sample concentrations ranged from 5 mg/dL to 158
   mg/dL as measured by the predicate device. These specimens were
   randomized and assayed using both the Envoy 500 HDL cholesterol
   application and the predicate device. The results, which spanned the full
   reportable range of the device, were compared by least squares regression.
   Regression statistics for the combined serum and plasma specimens are shown
   below.

   $$y = 0.7 \text{ mg/dL} + 1.021 \text{ x} \qquad r = 0.991$$

   b. *Matrix comparison:*

   Not applicable

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:

HDL cholesterol results should be evaluated against the risk classifications established by the National Cholesterol Education Program (Adult Treatment Panel III).[4] These classifications for adults are listed below.

Risk Classification	Conventional Units	SI Units
Low	< 40 mg/dL	< 1.04 mmol/L
High	≥ 60 mg/dL	≥ 1.55 mmol/L

[4] National Institutes of Health, National Cholesterol Education Program. Detection Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), Final Report. NIH Publication No. 02-5215, September 2002.

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.