510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203597

B Applicant

Abbott Ireland Diagnostics Division

C Proprietary and Established Names

Cholesterol2

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CHH	Class I, meets the limitations of exemption 21CFR 862.9(c)(4)	21 CFR 862.1175 - Cholesterol (Total) Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Cholesterol

C Type of Test:

Quantitative Enzymatic esterase-oxidase

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The Cholesterol2 assay is used for the quantitation of cholesterol in human serum or plasma on the ARCHITECT c System . The Cholesterol2 assay is to be used as an aid in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

For In Vitro Diagnostic Use Only

D Special Instrument Requirements:

For use on ARCHITECT c8000 System.

IV Device/System Characteristics:

A Device Description:
The Cholesterol2 reagent kits are available in two formats that allow for testing 1000 or 3200 samples. Each kit is comprised of one reagent:

Reagent 1: Active ingredients: cholesterol esterase 0.880 KU/L, cholesterol oxidase (CONII-FD) 0.330 KU/L, TODB 0.466 g/L, 4-aminoantipyrine 0.134 g/L and peroxidase (POD) 6.600 KU/L.
Preservative: Sodium azide.

The following are also required to conduct testing but are not provided with the kit:

- Cholesterol2 assay file found on www.corelaboratory.abbott
- 04V1501 Consolidated Chemistry Calibrator
- Controls containing cholesterol
- Saline (0.85% to 0.90% NaCl) for specimen dilution

B Principle of Operation:

Cholesterol esters are enzymatically hydrolyzed by cholesterol esterase to cholesterol and free fatty acids. Free cholesterol, including that originally present, is then oxidized by cholesterol oxidase to cholest-4-ene-3-one and hydrogen peroxide. The hydrogen peroxide oxidatively couples with N,N-Bis(4-sulfobutyl)-3-methylaniline (TODB) and 4-aminoantipyrine to form a chromophore (quinoneimine dye) which is quantitated at 604 nm.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Chol

B Predicate 510(k) Number(s):
K981652

C Comparison with Predicate(s):

Device & Predicate Device(s):	K203597	K981652
Device Trade Name	Cholesterol2	Chol
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the quantiation of cholesterol in human serum or plasma. To be used as an aid in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders.	Same
Analyte	Cholesterol	Same
Sample Type	Human Serum or Plasma	Same
Methodology	Enzymatic	Same
Standardization	Human Cholesterol (Abell-Kendall)	Same
Tube Types	Serum: - Serum tubes - Serum separator tubes Plasma: - Lithium heparin tubes - Lithium heparin separator tubes - Sodium heparin tubes	Same
General Device Characteristic Differences		
Analytical Measuring Interval (AMI)	5–748 mg/dL	7-705 mg/dL

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP07: Interference Testing in Clinical Chemistry-Third Edition

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures-Second Edition.

CLSI-EP35: Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures- First Edition

CLSI-EP37: Supplemental Tables for Interference Testing in Clinical Chemistry-First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Precision of the Cholesterol2 test system was evaluated according to CLSI EP05-A3. Two levels of controls and 3 levels of human serum samples were tested on 3 lots of reagent, 3 lots of calibrator, 1 lot of commercial controls, and 3 instruments. Two replicates of samples were tested on two runs per day for 20 days (n=80). The results of one representative lot are shown below:

Sample	n	Mean (mg/dL)	Within-Run (Repeatability)		Within-Laboratory[a]	
			SD	%CV	SD (Range[b])	%CV (Range[b])
Control Level 1	80	251	1.9	0.7	2.6 (2.6 - 3.1)	1.0 (1.0 – 1.2)
Control Level 2	80	106	1.0	1.0	1.3 (1.3 – 1.7)	1.2 (1.2 -1.6)
Serum Level 1	80	21	0.6	3.0	0.8 (0.7 – 0.8)	4.0 (3.2 – 4.1)
Serum Level 2	80	237	2.8	1.2	4.5 (3.7 – 4.9)	1.9 (1.5 – 2.0)
Serum Level 3	80	718	6.4	0.9	6.6 (4.6 – 6.9)	0.9 (0.7 – 1.0)

[a] Includes within-run, between-run, and between-day variability.
[b] Minimum and maximum SD or %CV across all reagent lot and instrument combinations.

2. Linearity:
A total of 15 samples were prepared for the linearity assessment with concentrations spanning the claimed measuring range, 5 to 748 mg/dL. Each level was analyzed in replicates of two using 1 lot of reagent, 1 lot of calibrator, 1 lot of control, and 1 instrument. Deviations from linearity within the claimed range were never observed to be greater than 5%.
The sponsor provided dilution studies which supported the measurement of samples above the measurement range diluted by a factor of 4.

3. Analytical Specificity/Interference:
Interference testing was performed based on guidance from CLSI EP07, 3rd ed. using 2 different concentrations of cholesterol (150 mg/dL and 220 mg/dL) with individual interferents at a range of concentrations. Samples were tested in replicates of 10 using one lot of reagent and one ARCHITECT c8000 analyzer. The following tables list the concentration of each substance at which no significant interference was detected; defined as a difference of less than or equal to ±10% between the test sample and control.

   a. Endogenous substances:
      i. No significant interference beyond ± 10% was observed at the following concentrations:

Potentially Interfering Substance	Interferent Level
Conjugated Bilirubin	7 mg/dL
Unconjugated Bilirubin	11 mg/dL
Hemoglobin	1000 mg/dL
Total Protein	15 g/dL

   b. Exogenous substances:
      i. All substances tested with two concentrations of analyte (cholesterol 150 and 220 mg/dL), except ascorbic acid and methyldopa, which were tested only at 150 mg/dL. No significant interference beyond ± 10% observed at the following concentrations:

Potentially Interfering Substance	Interferent Level
Acetaminophen	160 mg/L
Acetylcysteine	150 mg/L
Acetylsalicylic Acid	30 mg/L
Aminoantipyrine	40 mg/L
Ampicillin-Na	80 mg/L
Ascorbic Acid	55 mg/L
Biotin	4250 ng/mL
Ca-dobesilate	60 mg/L
Cefotaxime	53 mg/dL
Cefoxitin	6600 mg/L
Cyclosporine	2 mg/L
Desacetylcefotaxime	6 mg/dL

Potentially Interfering Substance	Interferent Level
Dipyrone	100 mg/L
Dobutamine	0.2 mg/dL
Doxycycline	20 mg/L
Ibuprofen	220 mg/L
Intralipid	1050 mg/dL
Levodopa	8 mg/L
Methotrexate	140 mg/L
Metronidazole	130 mg/L
Methylaminoantipyrine	40 mg/L
Methyldopa	20 mg/L
N-Acetyl-p-benzoquinone (NAPQI)	20 mg/L
Phenylbutazone	330 mg/dL
Phenytoin	6 mg/dL
Rifampicin	50 mg/L
Sodium Heparin	4 U/mL
Sulpiride	15 mg/L
Theophylline (1.3-dimethylxanthine)	60 mg/L

To address potential interference from conjugated and unconjugated bilirubin, the labeling contains the following statements:

- Specimens with conjugated bilirubin levels greater than 7 mg/dL or unconjugated bilirubin greater than 11 mg/dL may cause falsely depressed results with the Cholesterol2 assay. Refer to the SPECIFIC PERFORMANCE CHARACTERISTICS, Analytical Specificity, Interference section of this package insert. To estimate sample icterus levels, refer to the Sample Interference Indices instructions for use to assess hemolysis (H), icterus (I) and lipemia (L) (HIL) indices.

4. Assay Reportable Range:
   Based on the limit of detection (LoD), limit of quantitation (LoQ), precision, and linearity, the ranges over which results can be reported are provided below:

Analytical Measuring Interval (AMI)	5–748 mg/dL
Extended Measuring Interval (EMI)	748–2992 mg/dL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The Cholesterol2 reagent is certified to be traceable to the National Reference System for Cholesterol, against the Abell-Kendall reference method in a CDC-Certified Cholesterol Reference Method Laboratory Network (CRMLN).

6. Detection Limit:

   Determination of the limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) were conducted following the recommendations in the CLSI EP17-A2 guideline.

Limit of Blank:
The LoB was determined by testing 6 zero-analyte samples in replicates of 10 using 3 lots of reagent on 2 instruments across 3 days for a total 60 measurements. Using the parametric approach, LoB was derived from the 95th percentile of a normal distribution.

Limit of Detection:
The LoD was determined by testing 6 low-analyte level samples. Each sample was tested in replicates of 10 using 3 lots of reagent on 2 instruments across 3 days for a total 60 measurements. The parametric approach described in CLSI EP17-A2 was followed to determine the LoD.

Limit of Quantitation:
The LoQ was determined by testing two samples with low concentrations tested in replicates of 10 using 3 lots of reagent on 2 instruments across 3 days for a total of 60 measurements . The sponsor defined the LoQ as the lowest analyte concentration where the %CV was ≤ 20%.

The detection limit results are summarized as follows:

Analyte	LoB	LoD	LoQ
Cholesterol	1 mg/dL	2 mg/dL	5 mg/dL

7. Assay Cut-Off:
Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
A total of 138 serum patient samples spanning the range of 7 to 684 mg/dL were analyzed with the candidate cholesterol assay on the ARCHITECT c8000 versus the predicate device. Of the 138 samples, 14 samples were diluted or spiked. All samples were analyzed in singlicate. Results of the Passing-Bablok linear regression are presented below:

Cholesterol2 vs. Cholesterol on the ARCHITECT c System						
Serum	**Units**	**n**	**Correlation Coefficient**	**Intercept**	**Slope**	**Concentration Range**
	mg/dL	138	1.00	0.41	0.98	7-684

Predicted Bias at Medical Decision Points: An estimate of the predicated bias at the medical decision points was calculated as the percent difference between the regression line and the unity line at each medical decision point.

Predicated Bias at Medical Decision Points (95% confidence interval, CI)			
	170 mg/dL	200 mg/dL	240 mg/dL
Total Cholesterol	-1.8% (-3.1, -0.8)	-1.9% (-3.0, -0.9)	-1.9% (-3.0, -1.0)

An additional method comparison study was conducted to support accuracy at concentrations ranging from 700 to 748 mg/dL. Results from the candidate cholesterol assay on the ARCHITECT c800 were compared to the results obtained from a certified reference method. The high concentration samples demonstrated ≤ 2.4% bias from the reference method.

2. Matrix Comparison:
The matrix comparison study was performed using 60 samples of each sample type across the measurable range. The samples were analyzed on the ARCHITECT c8000 analyzer. Individual results of each matrix comparison study were compared to the reference results (Serum). The details and results of the study using simple linear regression analysis are as follows:

Sample Type	n	Intercept	Slope	R^2	Concentration Range (Serum)
Serum vs. Serum separator	60	0	1.00	1.00	20 – 730 mg/dL
Serum vs. Lithium heparin	60	-2	1.00	1.00	20 – 730 mg/dL
Serum vs. Lithium heparin separator	60	-2	1.00	1.00	20 – 730 mg/dL
Serum vs. Sodium heparin separator	60	-2	1.00	1.00	20 – 730 mg/dL

C Clinical Studies:

1. Clinical Sensitivity:
Not applicable.

2. Clinical Specificity:
Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):
Not applicable.

D Clinical Cut-Off:
Not applicable.

E Expected Values/Reference Range:
The clinical cut points* for total cholesterol was identified in the labeling as follows:

Serum/Plasma		Range (mg/dL)
Adult	Desirable	<200
	Borderline	200 - 239
	High	≥ 240
Child	Desirable	<170
	Borderline	170 - 199
	High	≥ 200

*Wu AHB, editor. Tietz Clinical Guide to Laboratory Tests. 4th ed. St. Louis, MO: Saunders Elsevier; 2006:244.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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