June 30, 2022

Abbott Ireland Diagnostics Division
Tracy Schmidt
Senior Specialist Regulatory Affairs
Lisnamuck, Longford
Co. Longford, Ireland

Re: K203597
Trade/Device Name: Cholesterol2
Regulation Number: 21 CFR 862.1175
Regulation Name: Cholesterol (total) test system
Regulatory Class: Class I, meets the limitation to the exemption 21 CFR 862.9(c)(4)
Product Code: CHH
Dated: March 25, 2022
Received: March 28, 2022

Dear Tracy Schmidt:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k203597

Device Name
Cholesterol2

Indications for Use *(Describe)*
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 an an aid in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary (Summary of Safety and Effectiveness)

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

I. 510(k) Number

k203597

II. Applicant Name

Abbott Ireland
Diagnostics Division
Lisnamuck, Longford,
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Ireland

Primary contact person for all communications:

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Date Summary Prepared: June 22, 2022.

III. Device Name

Cholesterol2

Reagents

Trade Name: Cholesterol2
Device Classification: Class I, meets the limitation of exemption per 21 CFR §862.9(c)(4)
Classification Name: Enzymatic esterase--oxidase, cholesterol
Governing Regulation Number: 21 CFR §862.1175
Product Code: CHH

IV. Predicate Device

Cholesterol (k981652)

V. Description of Device

A. Principles of the Procedure

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.

Methodology: Enzymatic

B. Reagents

The configurations of the Cholesterol2 reagent kits are described below.

Volumes (mL) listed in the following table indicate the volume per cartridge.

	List Number	
	04S9220	**04S9230**
Tests per cartridge	250	800
Number of cartridges per kit	4	4
Tests per kit	1000	3200
Reagent 1 (R1)	21.6 mL	62.5 mL

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 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).

VI. Intended Use of the Device

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.

VII. Comparison of Technological Characteristics

The Cholesterol2 assay (subject device) is an automated clinical chemistry assay for the quantitation of cholesterol in human serum or plasma on the ARCHITECT c System.

The similarities and differences between the subject assay and the predicate device are presented in the following table.

Comparison of Subject Device Cholesterol2 to Predicate Device Cholesterol

Characteristics	Subject Device Cholesterol2 (List No. 04S92)	Predicate Device Cholesterol (k981652; List No. 7D62)
Platform	ARCHITECT c8000 System	Same*
Intended Use and Indications 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.	The Cholesterol assay is used for the quantitation of cholesterol in human serum or plasma. Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders.
Methodology	Enzymatic	Same
Specimen Type	Human serum or plasma	Same
Assay Principle/ Principle of Procedure	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.	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 combines with hydroxybenzoic acid (HBA) and 4-aminoantipyrine to form a chromophore (quinoneimine dye) which is quantitated at 500 nm.
Standardization	Human cholesterol (Abell-Kendall)	Same
Use of Calibrators	Yes	Same
Use of Controls	Yes	Same
Assay Range	Analytical Measuring Interval (AMI): 5–748 mg/dL Extended Measuring Interval (EMI): 748–2992 mg/dL Reportable Interval: 2–2992 mg/dL	AMI: 7–705 mg/dL EMI: 705–2820 mg/dL

* In accordance with FDA Guidance Document "Data for Commercialization of Original Equipment Manufacturer, Secondary and Generic Reagent for Automated Analyzers", issued June 10, 1996, the assay equivalency study on ARCHITECT c System vs. the original platform, AEROSET, was performed and submitted under K980367/A004 in May 2002.

Characteristics	Subject Device Cholesterol2 (List No. 04S92)	Predicate Device Cholesterol (k981652; List No. 7D62)
Platform	ARCHITECT c8000 System	Same*
Precision	Samples with cholesterol concentrations between 21 and 718 mg/dL demonstrated standard deviations ranging from 0.7 to 6.9 mg/dL and % Coefficient of Variation (%CV) values ranging from 0.7 to 4.1%.	Samples with cholesterol concentrations between 129.2 and 261.4 mg/dL demonstrated standard deviations ranging from 2.09 to 4.03 mg/dL and % Coefficient of Variation (%CV) values ranging from 1.5 to 1.6%.
Lower Limits of Measurement	Limit of Blank: 0 mg/dL Limit of Detection: 2 mg/dL Limit of Quantitation: 5 mg/dL	Limit of Detection: 5.0 mg/dL Limit of Quantitation: 6.2 mg/dL
Tube Types	Serum: - Serum tubes - Serum separator tubes Plasma: - Lithium heparin tubes - Lithium heparin separator tubes - Sodium heparin tubes	Serum: Glass or plastic serum tubes with or without gel barriers Plasma: Glass or plastic tubes - Lithium heparin tubes (with or without gel barrier) - Sodium heparin tubes

VIII. Summary of Nonclinical Performance

All performance characteristics were obtained using the ARCHITECT c8000 System.

A. Reportable Interval

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 according to the definitions from CLSI EP34, 1st ed.*

	mg/dL
Analytical Measuring Interval (AMI)[a]	5–748
Extended Measuring Interval (EMI)[b]	748–2992

* Clinical and Laboratory Standards Institute (CLSI). *Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking.* 1st ed. CLSI Document EP34. Wayne, PA: CLSI; 2018.

Reportable Interval[c]	2–2992

[a] AMI: The AMI extends from the LoQ to the upper limit of quantitation (ULoQ). This is determined by the range of values in mg/dL that demonstrated acceptable performance for linearity, imprecision, and bias.

[b] EMI: The EMI extends from the ULoQ to the ULoQ × sample dilution.

[c] The reportable interval extends from the LoD to the upper limit of the EMI.

NOTE: The default Low Linearity value of the assay file corresponds to the lower limit of the analytical measuring interval. Samples with cholesterol values below 5 mg/dL are reported as "< 5 mg/dL".

B. Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A3.* Testing was conducted using 3 lots of the Cholesterol2 reagent, 3 lots of the Consolidated Chemistry Calibrator, and 1 lot of commercially available controls and 3 instruments. Two controls and 3 human serum panels were tested in duplicate, twice per day on 20 days on 3 reagent lot/calibrator lot/instrument combinations, where a unique reagent lot and a unique calibrator lot is paired with 1 instrument. The performance from a representative combination is shown in the following table.

			Within-Run (Repeatability)		**Within-Laboratory[a]**	
Sample	**n**	**Mean (mg/dL)**	**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)
Panel A	80	21	0.6	3.0	0.8 (0.7–0.8)	4.0 (3.2–4.1)
Panel B	80	237	2.8	1.2	4.5 (3.7–4.9)	1.9 (1.5–2.0)
Panel C	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.

* Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.

C. Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.* Testing was conducted using 3 lots of the Cholesterol2 reagent on each of 2 instruments over a minimum of 3 days. The maximum observed limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) values are summarized below.

	mg/dL
LoB[a]	0
LoD[b]	2
LoQ[c]	5

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met and was determined from n ≥ 60 replicates of low-analyte level samples.

D. Linearity

A study was performed based on guidance from CLSI EP06-A.≠

The assay was demonstrated to be linear across the analytical measuring interval of 5 to 748 mg/dL.

* Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.

≠ Clinical and Laboratory Standards Institute (CLSI). *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. CLSI Document EP06-A. Wayne, PA: CLSI; 2003.

E. Potentially Interfering Endogenous and Exogenous Substances

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.* Each substance was tested at 2 levels of the analyte (approximately 150 mg/dL and 220 mg/dL). **No significant interference (interference within ± 10%, based on 95% confidence intervals)** 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

Interference beyond ± 10% (based on 95% Confidence Intervals [CI]) was observed at the concentrations shown below for the following substance.

Potentially Interfering Substance	Interferent Level	Analyte Level	% Interference (95% CI)
Conjugated Bilirubin	40 mg/dL	150 mg/dL	-39% (-40%, -39%)
Conjugated Bilirubin	40 mg/dL	220 mg/dL	-31% (-31%, -30%)
Unconjugated Bilirubin	16 mg/dL	150 mg/dL	-11% (-11%, -10%)

* Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI Guideline EP07. Wayne, PA: CLSI; 2018.

Potentially Interfering Exogenous Substances

No significant interference (interference within ± 10%, based on 95% confidence intervals) was 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
Dipyrone	100 mg/L
Dobutamine	0.2 mg/dL
Doxycycline	20 mg/L
Ibuprofen	220 mg/L
Intralipid	1050 mg/dL

Potentially Interfering Substance	Interferent Level
Levodopa	8 mg/L
Methotrexate	140 mg/dL
Metronidazole	130 mg/L
Methylaminoantipyrine	40 mg/L
Methyldopa	20 mg/L
N-Acetyl-p-benzoquinone (NAPQI)	20 mg/L
Phenylbutazone	330 mg/L
Phenytoin	6 mg/dL
Rifampicin	50 mg/L
Sodium heparin	4 U/mL
Sulpiride	15 mg/L
Theophylline (1,3-dimethylxanthine)	60 mg/L

Interference beyond ± 10% (based on 95% Confidence Intervals [CI]) was observed at the concentrations below for the following substance.

Potentially Interfering Substance	Interferent Level	Analyte Level	% Interference (95% CI)
Ascorbic acid	60 mg/L	150 mg/dL	-10% (-11%, -10%)
Intralipid	2000 mg/dL	150 mg/dL	-27% (-27%, -28%)
Intralipid	2000 mg/dL	220 mg/dL	-22% (-21%, -23%)
Methyldopa	30 mg/L	150 mg/dL	-14% (-14%, -13%)

F. Method Comparison

A study was performed based on guidance from CLSI EP09-A3* using the Passing-Bablok regression method. The study compared the Cholesterol2 assay to the Cholesterol assay (List Number 7D62).

Cholesterol2 vs. Cholesterol on the ARCHITECT c8000 System

	Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Serum	mg/dL	138	1.00	0.41	0.98	7–684

G. Tube Type

A study was performed to evaluate the suitability of specific blood collection tube types for use with the Cholesterol2 assay. Samples were collected from a minimum of 40 donors and evaluated across tube types. The following blood collection tube types were determined to be acceptable for use with the Cholesterol2 assay:

Serum tubes
Serum separator tubes
Lithium heparin tubes
Lithium heparin separator tubes
Sodium heparin tubes

* Clinical and Laboratory Standards Institute (CLSI). *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. CLSI Document EP09-A3. Wayne, PA: CLSI; 2013.

H. Dilution Verification

A study was performed to evaluate the performance of the Cholesterol2 automated dilution protocol and the manual dilution procedure on the ARCHITECT c8000 System.

Eight human serum samples were created by spiking cholesterol stock solution into SeraSub (a synthetic serum) to target concentrations across the extended measuring interval (EMI) (805, 1000, 1250, 1500, 1800, 2000, 2500, and 2800 mg/dL) that were value assigned using the analytically validated method.

The automated dilution factor for the Cholesterol2 assay is 1:5.97.

The manual dilution factor of 1:4 was evaluated for the Cholesterol2 assay.

I. Certificate of Traceability

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).

IX. Summary of Clinical Performance

This section does not apply.

X. Conclusion Drawn from Nonclinical Laboratory Studies

The results presented in this 510(k) premarket notification demonstrate that the performance of the subject device, Cholesterol2 (List No. 04S92), is substantially equivalent to the predicate device, Cholesterol (List No. 7D62, k981652).

The similarities and differences between the subject device and predicate device are presented in Section 5-VII.

There is no known potential adverse effect to the operator when using this *in vitro* device according to the Cholesterol2 reagent package insert instructions.