510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K251091

B Applicant

Truvian Health

C Proprietary and Established Names

Lipids

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CHH	Class I, meets the limitations of exemptions in 862.9(c)(4)	21 CFR 862.1175 - Cholesterol (Total) Test System	CH - Clinical Chemistry
JGY	Class I, meets the limitations of exemptions in 862.9(c)(4)	21 CFR 862.1705 - Triglyceride test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Cholesterol
Triglycerides

C Type of Test:

Quantitative, photometric/colorimetric

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Lipids is part of TruWellness Panel™ and is intended for use on the TruVerus. Lipids (part of the TruWellness Panel) is an in-vitro diagnostic device and intended to be used for the quantitative determination of Total Cholesterol (TChol) and Triglycerides (TRIG) in lithium-heparinized venous whole blood in clinical laboratory or point-of-care settings. From TRIG determination, Very Low-Density Lipoprotein (VLDL) is calculated by the analyzer. Lipids (part of the TruWellness Panel) is an in vitro diagnostic test system that aids the physician in diagnosis and treatment of the following disorders:

Total Cholesterol (TChol): Excess cholesterol in the blood and lipid and lipoprotein disorders.

Triglyceride (TRIG): Diabetes mellitus, nephrosis, liver obstruction, and other diseases involving lipid metabolism; various endocrine disorders.

C Special Conditions for Use Statement(s):

Rx- For Prescription Use Only

Lipids (part of the TruWellness panel) is intended for use with adults aged 18 and older.

The Triglyceride analyte is sensitive to Icterus and is not for use with patients with hyperbilirubinemia (elevated bilirubin levels).

The instrument was validated up to an altitude of 2,000 m (6562 ft). Lipids should not be used above 2,000 m (6562 ft).

D Special Instrument Requirements:

TruVerus was cleared under K251058 with the trade name Tru Analyzer.

IV Device/System Characteristics:

A Device Description:

Lipids contains the following reagents:

Component	Quantity per Kit
4-Aminoantipyrine	5.6 µg
Adenosine-5'-Triphosphate	17.5 µg

Component	Quantity per Kit
Catalase	21.5 U
Cholesterol Esterase	≥ 21.9 mU
Cholesterol Oxidase	≥ 15.4 mU
Glycerol Kinase	≥ 19.1 mU
Glycerol Phosphate Oxidase	≥ 57.3 mU
HDAOS	4.7 µg
Peroxidase	> 975.0 mU
p-Hydroxybenzenesulfonate	31.6 µg
Sodium N-Ethyl-N-(3-Sulfopropyl)-M-Anisidine	5.6 µg

The Single-Use Consumable Kit houses all the components needed to process as well as analyze samples on the TruVerus, including dried reagents, internal process control solutions, barcodes that manage the identity of the kit lot (e.g., Disc and Support Pack ID), calibration information, dilution buffers, and single-use plastic pipette tips. It also serves as a waste container which the user discards of at the end of the run. The Support Pack contains a feature to accept a standard 4 mL blood tube. The Support Pack also houses 22 pipette tips for transferring and mixing samples and reagents, 11 dilution wells to support reagent processing activities within the test system (e.g., sample dilution, reagent dilution, rehydration of dried reagents), and 6 x 2 mL tubes that contain additional wet and dry reagents.

B Principle of Operation:

Total cholesterol

This assay is based on the work of Allain et al. and measures the total level of cholesterol by using a multi-step enzymatic system. Cholesterol esters are hydrolyzed by cholesterol esterase to cholesterol and fatty acids. Cholesterol is oxidized by cholesterol oxidase to Δ4-cholestenone with the simultaneous production of an equimolar amount of hydrogen peroxide. In the presence of peroxidase, hydrogen peroxide oxidizes to p-hydroxybenzenesulfonate (p-HBS) and 4-aminoantipyrine (4-AAP) to give a quinoneimine dye colored red, the absorbance of which can be measured at 510 nm. The absorbance is proportional to the concentration of cholesterol in the sample.

Triglycerides

This assay measures triglyceride concentration in plasma by a series of enzymatic reactions. After hydrolysis by microbial lipases, the triglycerides yield glycerol and free fatty acids (FFA). Glycerol is phosphorylated by adenosine-5'-triphosphate (ATP) to glycerol-1-phosphate (G-1-P) in a reaction catalyzed by glycerol kinase (GK). G-1-P is oxidized to dihydroxyacetone phosphate (DAP) in a reaction catalyzed by glycerol phosphate oxidase (GPO). In this reaction, hydrogen peroxide is produced in equimolar concentration to the level of triglycerides present in the sample. In the indicating Trinder type reaction, hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) and n-ethyl-n-(3-sulfopropyl)-m-anisidine (ESPAS) in a reaction catalyzed by peroxidase (HPOD). The result of this oxidative coupling is a quinoneimine red-colored dye the absorbance of which can be measured at 540 nm. The absorbance is proportional to the concentration of triglycerides in the sample.

Very low-density lipoprotein (VLDL) cholesterol

VLDL cholesterol is calculated using the following equation that utilizes the triglyceride measurement: VLDL Cholesterol = Triglyceride/5 (if units in mg/dL).

V Substantial Equivalence Information:

A Predicate Device Name(s):

Piccolo Total Cholesterol Test System – K023642
Piccolo Triglycerides Test System – K023639

B Predicate 510(k) Number(s):

K023642 and K023639

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251091 Candidate	K023642 Predicate
Device Trade Name	Lipids	Piccolo Total Cholesterol Test System
General Device Characteristic Similarities		
Intended Use/Indications For Use	In vitro quantitative determination of Total Cholesterol and Triglycerides (TRIG) in heparinized whole blood in clinical laboratory setting or point-of-care location.	Same
Measuring Range	TChol: 20 - 520 mg/dL	Same
General Device Characteristic Differences		
Sample type	Lithium-heparinized venous whole blood	Heparinized whole blood, heparinized plasma, and serum

Device & Predicate Device(s):	K251091 Candidate	K023639 Predicate
Device Trade Name	Lipids	Piccolo Triglycerides Test System
General Device Characteristic Similarities		
Intended Use/Indications For Use	In vitro quantitative determination of Total Cholesterol and Triglycerides (TRIG) in heparinized whole blood in clinical laboratory setting or	Same

	point-of-care location.	
General Device Characteristic Differences		
Sample type	Lithium-heparinized venous whole blood	Heparinized whole blood, heparinized plasma, and serum
Measuring Range	20 - 700 mg/dL	20 - 500 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 EP06 Ed.2, Evaluation of the Linearity of Quantitative Measurement Procedures

CLSI EP07 Ed.3, Interference Testing in Clinical Chemistry

CLSI EP09c Ed.3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition

CLSI EP25 Ed.2, Evaluation of Stability of In Vitro Medical Laboratory Test Reagents

CLSI EP37 Ed.1, Supplemental Tables for Interference Testing in Clinical Chemistry

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A. Reproducibility with control materials.
This study was designed according to CLSI EP05-A3. The study was conducted at 3 external point-of-care (POC) sites, with 3 analyzers per site and at least 3 POC operators per site. Testing was conducted over 5 days using a single lot of consumables and consisted of 3 levels of control samples at low, medium, and high concentrations, with 6 replicates run per day, 3 run in the morning and 3 run in the afternoon (each replicate is run on an individual instrument). Overall, there were at least 90 replicates for each precision control sample level (3 sites x 1 sample x 3 replicates per run x 2 runs per day x 5 days = 90 replicates). The total precision as well as within run, between day, and between site precision were estimated. Results are displayed below.

Analyte	Level	N	Mean	Within - Run		Between-Run		Between-Day		Between-Site		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
TChol	Low	92	82	2	2.6	0	0.0	0	0.0	1	1.5	2	3.0
TChol	Med	91	189	4	2.3	1	0.4	0	0.0	2	1.0	5	2.6
TChol	High	92	228	3	1.5	0	0.0	0	0.0	2	1.1	4	1.9
TRIG	Low	92	88	2	1.8	0	0.0	0	0.0	1	0.9	2	2.0
TRIG	Med	91	136	3	2.1	1	0.4	1	0.6	0.4	0.3	3	2.2
TRIG	High	92	452	5	1.1	0	0.0	1	0.3	1	0.2	5	1.1

B. Whole blood precision

This study was evaluated at five sites collecting samples from intended use population with normal and abnormal analyte levels. At least 20 subjects were enrolled at each site and for each test subject, eight replicates were measured across four instruments and two operators. The SD and CV% were calculated by pooling subject standard deviations and/or % CV for predefined Low, Medium, and High sub-intervals selected to represent normal and abnormal regions of the analytical measuring range and encompassing medical decision levels. Pooled imprecision is considered a representative estimate of reproducibility that include variability of sites, instruments, operators, days and repeatability.

Analyte	Range (mg/dL)	Subjects (N)	Mean (mg/dL)	SD	CV%
TChol	20–200	93	139	3.5	2.5
TChol	200–240	10	214	4.8	2.3
TChol	240–520	9	313	8.2	2.6
TRIG	20–150	69	91	2.2	2.9
TRIG	150–250	25	184	3.6	1.9
TRIG	250–700	9	339	5.7	1.6

C. Whole blood between-lot precision.

22 subjects consisting of 6 healthy individuals and 16 individuals in various disease states were enrolled at a single point-of-care clinical site and tested across 3 lots of the candidate panel on 3 individual analyzers by 2 operators. A total of 6 replicates per subject participant, 2 replicates per lot, were tested by 1 of the 2 operators. Results below present the number of subjects evaluated, the % difference from the mean and pooled %CV by lot and by analyte.

Analyte	N-Subjects Per Lot	Mean relative difference %			Pooled %CV		
		Lot-A	Lot-B	Lot-C	Lot-A	Lot-B	Lot-C
TCHOL	22	-0.5%	-0.5%	1.0%	2.6 %	2.1 %	1.9 %
TRIG	21	0.7%	-0.7%	0.0%	2.5 %	2.0 %	1.8 %

D. Control between-lot reproducibility.

To evaluate the lot-to-lot reproducibility for the assays, three (3) control samples (Low, Medium, High) were tested on 3 analyzers with 3 lots of the candidate test. Each sample level was tested with at least five (5) replicates on one analyzer each day with each single-use consumable kit lot

over three (3) days to achieve a minimum of fifteen (15) replicates per sample level and kit lot. Results are displayed below:

Analyte	Sample	Units	N	Mean	SD			CV%		
					Lot 1	Lot 2	Lot 3	Lot 1	Lot 2	Lot 3
TChol	Low	mg/dL	45	84.5	2.25	1.40	2.13	2.7%	1.7%	2.5%
TChol	Medium	mg/dL	45	193.8	2.32	3.77	3.33	1.2%	1.9%	1.7%
TChol	High	mg/dL	45	231.7	3.27	5.56	3.07	1.4%	2.4%	1.3%
Trig	Low	mg/dL	45	89.3	1.43	1.83	1.84	1.6%	2.1%	2.0%
Trig	Medium	mg/dL	45	138.3	1.59	1.81	1.67	1.2%	1.3%	1.2%
Trig	High	mg/dL	45	454.4	4.29	12.42	3.73	0.9%	1.0%	0.8%

2. Linearity:

Linearity testing was performed in accordance with CLSI document EP06-Ed2. Linearity was assessed using multiple panels of samples. The linear range for total cholesterol and triglycerides were determined by testing nine (9) whole blood samples containing varying concentrations of analyte. Each sample was tested in quadruplicate, using one (1) kit lot, across four (4) analyzers, on a single day. The results of the study supported the claimed linear interval for TChol and Trig. Within the claimed analytical measuring range, the maximum observed deviation from linearity for TChol and TRIG were <2% and < 4% respectively.

3. Analytical Specificity/Interference:

Potential interference from endogenous and exogenous substances with the assays was evaluated following CLSI EP07-A3 and EP37 guidelines. Testing was performed with contrived lithium heparin whole blood samples from healthy donor population using two (2) analyte concentration levels targeted based on the recommendation in CLSI EP07. Endogenous and exogenous substances were spiked into samples at two targeted analyte concentration levels: approximately 150 mg/dL and 220 mg/dL for TChol, 100 mg/dL and 250 mg/dL for TRIG. For substances identified as an interferent, dose response testing was conducted to assess the highest concentration limit below which no significant interference was observed. Interference is defined as the analyte result shifted by more than 10% between the test and control samples*.

Endogenous Substances

Substance	Maximum Concentration without Interference (mg/dL)		
	Total Cholesterol	Triglyceride	
Hemoglobin	122	154	
Conjugated Bilirubin	4.1	< 200	2.1*
		> 200	2.3
Unconjugated Bilirubin	5.0	< 200	2.1
		> 200	4.9
Triglycerides	1814	N/A	

* Low level Conjugated Bilirubin testing showed ≤11% bias

Exogenous Substances

Substance	Max Concentration without Interference (mg/dL)	
	Total Cholesterol	Triglycerides
Acetaminophen	15.6	15.6
Acetylsalicylic acid	3	3
Ampicillin	7.5	7.5
Cefoxitin	495	660
Cyclosporine	0.18	0.18
Doxycycline	1.8	1.8
Heparin	3,300 U/L	3,300 U/L
Ibuprofen	10.95	21.9
Levodopa (L-Dopa)	0.75	0.3
Methyldopa	1.12	0.78
Metronidazole	12.3	12.3
Phenylbutazone	16.05	24.08
Rifampicin	4.8	4.8
Theophylline	6	6
Acetylcysteine	15	5
Ascorbic Acid	5.25	1.75
Calcium Dobesilate	3	1.5
Acetoacetate	20	20
Atorvastatin	0.075	0.075
Beta-Hydroxybutyrate	333	750
Caffeine	10.8	10.8
Cefotaxime	52.8	52.8
Cephalothin (Keflin)	180	180
Cimetidine	3	3
Creatinine	15	15
Cysteine	10	5
Digoxin	0.0039	0.0039
Dipyrone	3.3	3.3
Dobutamine	0.121	0.121
Fenofibrate	4.5	4.5
Fructose	18	18
Gemfibrozil (Lopid)	13.8	13.8
Glutathione	15	3.75
Isoniazide	6	6
Lactate Lithium	90	90
Lactose	100	100
Lidocaine	1.5	1.5
Lovastatin (Mevacor)	0.021	0.021
Methotrexate	102	54.4
Nicotinic Acid (Niacin)	10	10

Substance	Max Concentration without Interference (mg/dL)	
	Total Cholesterol	Triglycerides
Phenytoin	6	6
Pravastatin	0.0207	0.0207
Rosuvastatin	0.0111	0.0111
Salicylic Acid	2.86	2.86
Simvastatin	0.168	0.168
Sodium Methicillin	7.5	7.5
Urea	120	120
Uric Acid	23.5	23.5

The sponsor provided adequate information to support hemolysis, icterus and lipemia flags will detect samples subject to these interferences.

4. Assay Reportable Range:

The TruVerus Analyzer will report results within the AMR as listed in the table below.

Analyte	AMR
Total Cholesterol (mg/dL)	20–520
Triglycerides (mg/dL)	20–700

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

Traceability

The sponsor claims the following regarding traceability:

Assay	Traceable Material
Total Cholesterol	NIST SRM1950
Triglycerides	IFCC through commercial materials

Sample Stability
Sample stability studies performed demonstrated that samples measured on the candidate tests are stable for 60-minutes post-collection.

Open Pouch Stability and Open Disc Stability
The open disc stability study supports an open disc stability of 4 minutes when used on TruVerus at the following operating condition limits: 15°C - 30°C and 8% - 60% RH.

6. Detection Limit:

Detection limits were determined in accordance with recommendations in the CLSI EP17-A2 guideline.

The Limit of Blank (LoB) corresponds to the highest measurement result that is likely to be observed for a blank sample. The assay is designed to have a LoB ≤ Limit of Detection (LoD).

The Limit of Detection (LoD) corresponds to the lowest concentration of analyte that can be detected with a probability of 95%. The assay is designed to have an LoD ≤ Limit of Quantitation (LoQ).

The Limit of Quantitation (LoQ) corresponds to the lowest concentration of analyte in a sample that had a CV ≤ 20%. Detection limits are provided in the table below.

LoD and LoQ were established in Li-Hep whole blood samples.

Analyte	LoB	LoD	LoQ
Total Cholesterol (mg/dL)	3.76	6	7
Triglycerides (mg/dL)	12.45	14	16

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Whole blood specimens were collected from subjects at five external sites to evaluate the accuracy of the Lipids test. Specimens comprised of apparently healthy patient samples and samples from patients with acute or chronic health conditions were collected from 5 point-of-care sites, tested by at least 3 point-of-care operators per site, on at least 4 analyzers per site, using 10 lots of reagents. Results (using Passing Bablok regression) compared against a legally marketed comparator are displayed below. The data demonstrated that accuracy was consistent across sites.

Analyte	N	Range (mg/dL)	Slope	Intercept	R
TChol	326	23 – 475	1.00 (0.98, 1.01)	-4.00 (-5.0, -1.43)	0.995
Trig	313	29-683	1.00 (0.99, 1.01)	-6.00 (-6.05, -4.26)	0.998

Predicted Differences at Medical Decision Levels (MDLs)

		All	
	MDL (mg/dL)	**Bias**	**%Bias**
Total CHOL	**90**	-4.0	-4.4%
	200	-4.0	-2.0%
	240	-4.0	-1.7%

		All	
	MDL (mg/dL)	**Bias**	**%Bias**
TRIG	**150**	-6.0	-4.0%
	400	-6.0	-1.5%
	500	-6.0	-1.2%

2. Matrix Comparison:

Not applicable.

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):

High Altitude Study
An altitude study was conducted to evaluate the Lipids test at sea-level and a high altitude of 2000 meters. The results demonstrated acceptable performance at both tested altitude conditions.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

The sponsor provided the following risk classification intervals for TChol and TRIG based on scientific literature[1].

Analyte		**Reference Range (mg/dL)**
Total Cholesterol	Desirable	<200
	Borderline	200 - 239
	High	≥ 240
Triglycerides	Normal	< 150
	Borderline High	150 – 199
	High	200 – 499

Analyte		Reference Range (mg/dL)
	Very High	≥ 500

[1]*National Cholesterol Education Program. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). National Institutes of Health, National Heart, Lung, and Blood Institute, NIH Publication No. 01-3670, May 2001.*

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.