

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

A. 510(k) Number:

k080623

B. Purpose for Submission:

New Device

C. Measurand:

Cholesterol and Triglycerides

D. Type of Test:

Colorimetry

E. Applicant:

JAS Diagnostics, Inc.

F. Proprietary and Established Names:

Cholesterol Oxidase JAS; Glycerol Kinase, Triglycerides

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CHH - Enzymatic Esterase--Oxidase, Cholesterol	Class I (meets the limitation to exemptions in 21 CFR 862.9(c)(4))	21 CFR 862.1175 - Cholesterol (Total) Test System.	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
CDT - Lipase Hydrolysis/Glycerol Kinase Enzyme, Triglycerides	Class I (meets the limitation to exemptions in 21 CFR 862.9(c)(4))	21 CFR 862.1705 - Triglyceride Test System	75 Clinical Chemistry(CH)

H. Intended Use:

1. Intended use(s):

Refer to Indications for Use

2. Indication(s) for use:

Cholesterol Oxidase:

For the quantitative measurement of total cholesterol in serum. Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders. For in-vitro use only.

Triglycerides:

For the quantitative measurement of triglycerides in serum. Triglycerides measurements are used in the diagnosis and treatment of patients with diabetes

mellitus, nephrosis, liver obstruction and other diseases involving lipid metabolism or various endocrine disorders. For in-vitro use only.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

For use with the Synchron CX systems

I. Device Description:

Cholesterol Oxidase Reagent is available as a kit only. It consists of reagents with active ingredients, 4-Aminoantipyrine (0.25 mM), Cholesterol Oxidase (400 U/L), Lipoprotein Lipase (300 U/L), Horseradish Peroxidase (1000 U/L), HBA (10 mM), Surfactant, and Buffer pH (6.55 – 6.95).

Triglycerides Reagent is available as a kit only. It consists of reagents with active ingredients, ATP (2.5 mM), Magnesium Salt (2.6 mM), 4-Aminoantipyrine (0.8 mM), 3,5 DHBS (1.0 mM), GPO (Microbial) (11,000 U/L), Lipoprotein Lipase (microbial) (4,400 U/L), GK (Microbial) (660 U/L), Peroxidase (Horseradish) (2,900 U/L), and Buffer (50 mM).

J. Substantial Equivalence Information:

1. Predicate device name(s):

Synchron Systems Cholesterol Reagent; Beckman Synchron (Tm) Triglycerides Reagent

2. Predicate 510(k) number(s):

k971505; k915084

3. Comparison with predicate:

Characteristics	JAS Cholesterol Reagent (Proposed Device)	Beckman Synchron CX Reagent (Predicate Device)
Intended Use	For the in-vitro quantitative determination of Total Cholesterol in serum.	When used in conjunction with Synchron CX System, and Synchron CX Multi Calibrator, is intended for the quantitative determination of Cholesterol in human serum or plasma.
Methodology	Enzymatic Colorimetric Endpoint reaction	“Timed Endpoint” Enzymatic Colorimetric Endpoint reaction
Reagent Format	Reagent is supplied in a ready to use form.	No preparation is required.
Stability / Storage	Reagent is stable until the expiration date when stored at 2-8°C. Shelf life is 18 months when stored at 2-8°C.	Reagent when stored unopened at 2-8°C will obtain the shelf life indicated on the label. Once opened the reagent is stable for 30 days at 2-8°C unless expiration date is exceeded. DO not freeze. Specific shelf life is not indicated.

Sample / Reagent Ratio	1:100	1:100
Specimens	Serum	Serum or plasma
Linearity	8 – 730 mg/dL	5 – 750 mg/dL
Limit of Detection	1 mg/dL	5 mg/dL
Interference	<p>Bilirubin: 4.5 mg/dL (<10% or 3 mg/dL)</p> <p>Lipemia: 1020 mg/dL (<10% or 3 mg/dL)</p> <p>Hemolysis: 400 mg/dL (<10% or 3 mg/dL)</p>	<p>Bilirubin: Tested to 30 mg/dL < 25 @ 400 mg/dL</p> <p>Lipemia: Tested to 500 mg/dL NSI (+ 6% or 10.0 mg/dL)</p> <p>Hemolysis: Tested to 500 mg/dL NSI (+ 4.8% or 8.0 mg/dL)</p>
Reference Interval	<p>Desirable Cholesterol: <200 mg/dL</p> <p>Borderline-High Cholesterol: 201 – 239 mg/dL</p> <p>High Cholesterol: >240 mg/dL</p>	<p>Desirable Cholesterol: <200 mg/dL</p> <p>Borderline-High Cholesterol: 201 – 239 mg/dL</p> <p>High Cholesterol: >240 mg/dL</p>

Characteristics	JAS Triglycerides Reagent (Proposed Device)	Beckman Synchron CX Reagent (Predicate Device)
Intended Use	For the in-vitro quantitative determination of Triglycerides in serum.	When used in conjunction with Synchron CX System, and Synchron CX Multi Calibrator, is intended for the quantitative determination of Triglycerides concentration in human serum or plasma.
Methodology	Enzymatic Colorimetric Endpoint reaction	“Timed Endpoint” Enzymatic Colorimetric Endpoint reaction
Reagent Format	Reagent is supplied in a ready to use form.	Transfer all contents of compartment C to compartment A
Stability / Storage	Reagent is stable until the expiration date when stored at 2-8°C. Shelf life is 18 months when stored at 2-8°C.	Reagent when stored unopened at 2-8°C will obtain the shelf life indicated on the label. Once opened the reagent is stable for 30 days at 2-8°C unless expiration date is exceeded. DO not freeze. Specific shelf life is not indicated.
Sample / Reagent Ratio	1:100	1:100
Specimens	Serum	Serum or plasma

Linearity	5 – 800 mg/dL	10 – 1000 mg/dL
Limit of Detection	5 mg/dL	10 mg/dL
Interference	Bilirubin: Do not use visibly icteric samples. Hemolysis: 300 mg/dL ($\leq 10\%$ or 3 mg/dL)	Bilirubin: 5 mg/dL Observed effect ($\leq - 8.0$ mg/dL) Hemolysis: 500 mg/dL Observed effect ($\leq \pm 5.0$ mg/dL)
Reference Interval	Normal: <150 mg/dL Borderline: 150 – 199 mg/dL High: 200 – 499 mg/dL Very High: ≥ 500 mg/dL	Normal: <150 mg/dL Borderline: 150 – 199 mg/dL High: 200 – 499 mg/dL Very High: ≥ 500 mg/dL

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

CLSI EP-5A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

Cholesterol in the presence of oxygen is converted to Cholest-4-en-3-one hydrogen peroxide by the action of Cholesterol Oxidase. The hydrogen peroxide formed reacts with peroxidase and yields a red pigment Quinoneimine in the presence of HBA and AAP. The cholesterol concentration is obtained by measuring the absorbance of the red color at 540-550 nm. The absorbance of the color is proportional to the cholesterol concentration.

Triglycerides in the sample are hydrolyzed by lipase to glycerol and fatty acids. The glycerol is then phosphorylated by adenosine-5-triphosphate (ATP) to glycerol-3-phosphate (G3P) and adenosine-5-diphosphate in a reaction catalyzed by glycerol kinase (GK). Glycerol-3-phosphate is then converted to dihydroxyacetone phosphate (DAP) and hydrogen peroxide by glycerophosphate oxidase (GPO). The hydrogen peroxide then reacts with 4-aminoantipyrine (4-AAP) and 3,5 dichloro-2-hydroxybenzene (3,5DHBS) in a reaction catalyzed by peroxidase to yield a red colored quinoneimine dye. The triglyceride concentration is obtained by measuring the absorbance of the red color at 540-550 nm. The absorbance of the color is proportional to the triglycerides concentration.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated using serum-based control samples following recommendations in CLSI EP-5A2. Studies were conducted at one site over 20-day period with each sample tested 2 times per run and 2 runs per day. Three levels of serum-based controls previously cleared by FDA were tested.

Precision was evaluated using Synchron CX5 instrument and the results are given below.

Cholesterol Reagent		Within-Run		Total	
Specimen/Expected range (mg/dL)	Mean value and Range (mg/dL)	SD	CV (%)	SD	CV (%)
Control serum level 1	141.6	1.8	1.3	2.9	2.1
Control serum level 2	202	2.0	1.0	2.4	1.2
Control serum level 3	238.3	2.5	1.0	2.9	1.2

Triglycerides Reagent		Within-Run		Total	
Specimen/Expected range (mg/dL)	Mean value and Range (mg/dL)	SD	CV (%)	SD	CV (%)
Control serum level 1	51.8	1.3	2.6	1.9	3.7
Control serum level 2	156.1	2.8	1.8	3.9	2.5
Control serum level 3	266.1	3.1	1.2	4.0	1.5

b. Linearity/assay reportable range:

For the cholesterol oxidase reagent, the sponsor reported linearity and reportable range data using Synchron CX5 instrument. The linearity test panel consisted of 10 concentration levels distributed through an approximate range of 5 – 740 mg/dL. Each test level was run in duplicate on the above analyzer. Based on a linear regression analysis conducted for measured and assigned values, the Cholesterol assay demonstrated linearity with the equation, $y=1.094x-1.6$. The sponsor established the assay reportable range for serum at 8 – 730 mg/dL.

For the triglyceride reagent, the sponsor reported linearity and reportable range data for Synchron CX5 instrument. The linearity test panel consisted of 9 concentration levels distributed across an approximate range of 3 – 835 mg/dL. Each test level was run in duplicate on the above analyzer. Based on a linear regression analysis conducted for measured and assigned values, the Triglyceride assay demonstrated linearity with the equation, $y=0.988x+0.2$. The sponsor established the assay reportable range for serum at 5 – 800 mg/dL.

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

The sponsor uses calibrator and controls previously cleared (k981339) and are supplied separately from the kit. To ensure adequate quality control, the sponsor recommends running two quality controls, along with the samples.

d. Detection limit:

The sponsor evaluated the Limit of Detection (LoD), Limit of Quantitation (LoQ), and Limit of Blank (LoB) on Synchron CX5 instrument for the cholesterol reagent following the guidelines in CLSI EP17-A. Based on the evaluation of 90 blank (saline) and 30 low-level (4 mg/dL) sample values, the LoD was established at 2 mg/dL following the algorithm, $\text{LoD} = \text{mean of blank} + (1.6455 \times \text{SD of blank}) + (1.645 \times \text{SD of Low sample})$. Using 30 low level samples, the LoQ was established at 3.82 mg/dL.

The sponsor evaluated the Limit of Detection (LoD), Limit of Quantitation (LoQ), and Limit of Blank (LoB) on Synchron CX5 instrument for triglycerides following the guidelines in CLSI EP17-A. Based on the evaluation of 90 blank (saline) and 30 low-level (4 mg/dL) sample values, the LoD was established at 5 mg/dL following the algorithm, $\text{LoD} = \text{mean of blank} + (1.6455 \times \text{SD of blank}) + (1.645 \times \text{SD of Low sample})$. Using 30 low level samples the LoQ was established at 9.56 mg/dL.

e. Analytical specificity:

The sponsor evaluated the effect of hemoglobin (0-1000 mg/dL), free bilirubin (0 – 41.6 mg/dL), and lipemia (0-1147 mg/dL - tested only for cholesterol) on normal serum samples with cholesterol (~125 mg/dL) and triglyceride (~80 mg/dL) spiked with the interferents, and then compared with unspiked control. Based on the sponsor-defined interference limit of $\pm 10\%$ of control, the following interference limit claims were set by the sponsor for Synchron instrument tested. The sponsor's test results for unconjugated bilirubin demonstrated high interference for bilirubin at levels as low as 4.5 mg/dL for cholesterol and every level tested for triglycerides. The sponsor indicated in the labeling that users should not use any visibly icteric samples. The sponsor did not conduct studies to evaluate the interference from different drugs.

Interferent	No Interference claim up to (mg/dL)	
	Cholesterol	Triglyceride
Hemoglobin	400	300
Lipemia	1020	-
Unconjugated bilirubin	4.5	Fail at every level

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Performance of the Cholesterol oxidase reagent was compared with the predicate device, Synchron Systems Cholesterol Reagent (k971505) using Synchron CX5 system. Seventy two samples (sample range 11 – 694 mg/dL) including 2 diluted and 3 spiked samples were tested to cover the entire measuring range. Performance of the Triglyceride reagent was compared with the predicate device, Beckman Synchron (Tm) Triglycerides Reagent (k915084) using Synchron CX5 system. Sixty seven samples (sample range 6.0 – 763 mg/dL) including 4 diluted and 2 spiked samples were tested to cover the entire measuring range. Summaries of the sample number, composition, and the results of linear regression analysis for cholesterol and triglycerides are given below.

Device	Sample no.	Slope	Intercept (mg/dL)	r
Cholesterol	72	0.9217 (0.9076 – 0.9358)	-0.1	0.9979
Triglyceride	67	0.9319 (0.9150 – 0.9489)	-1.3	0.9972

These Cholesterol and Triglyceride assays have not been tested or certified by the Cholesterol Reference Method Laboratory Network (CRMLN).

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):

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The expected values of cholesterol and triglycerides were based on literature*. The sponsor states that they provide these ranges for reference only and each laboratory should establish its own normal range.

Sex	Expected Values for Cholesterol	Expected Values for Triglycerides
Desirable	< 200 mg/dL	< 150 mg/dL
Borderline high	200 – 239 mg/dL	150 – 199 mg/dL
High	>240 mg/dL	200 – 499 mg/dL
Very High	-	≥ 500 mg/dL

* National Institute of Health Publication No.01-3670, 3rd Report of NCEP Expert Panel on Detection, Evaluation, & Treatment of High Cholesterol in Adults (Adult Treatment Panel III) May (2001).

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.