

**SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k103747

B. Purpose for Submission:

New device

C. Measurand:

HDL and LDL Cholesterol

D. Type of Test:

Colorimetric enzymatic assay

E. Applicant:

SEPPIM S.A.S.

F. Proprietary and Established Names:

1. ELITech Clinical Systems CHOLESTEROL HDL SL 2G
2. ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR
3. ELITech Clinical Systems CHOLESTEROL LDL SL 2G
4. ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR
5. ELITech Clinical Systems ELITROL I and ELITROL II

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LBS	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1475 LDL & VLDL Precipitation, Cholesterol Via Esterase-Oxidase, HDL	Clinical Chemistry (75)
JIT	Class II	21 CFR 862.1150 Calibrator	Clinical Chemistry (75)
JJY	Class I, reserved	21 CFR 862.1660 Quality Control Material	Clinical Chemistry (75)
MRR	Class I, meets limitations per 21 CFR	21 CFR 862.1475 System, Test, Low Density, Lipoprotein	Clinical Chemistry (75)

	862.9(c)(4)		
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H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The ELITech Clinical Systems CHOLESTEROL HDL SL 2G assay is intended for use with ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR and ELITech Clinical Systems ELITROL I and ELITROL II on Vital Scientific Selectra/Flexor analyzers for the quantitative *in vitro* diagnostic determination of High Density Lipoprotein (HDL) Cholesterol in human serum and plasma. It is not intended for point of care settings. .

Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR is a calibrator for *in vitro* diagnostic use in the calibration of quantitative ELITech Clinical Systems CHOLESTEROL HDL SL 2G on the Vital Scientific Selectra Junior Analyzer and the Vital Scientific Flexor Junior Analyzer.

The ELITech Clinical Systems CHOLESTEROL LDL SL 2G assay is intended for use with ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR and ELITech Clinical Systems ELITROL I and ELITROL II on Vital Scientific Selectra/Flexor analyzers for the quantitative *in vitro* diagnostic determination of Low Density Lipoprotein (LDL) Cholesterol in human serum and plasma. It is not intended for point of care settings.

Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR is a calibrator for *in vitro* diagnostic use in the calibration of quantitative ELITech Clinical Systems CHOLESTEROL LDL SL 2G on the Vital Scientific Selectra Junior Analyzer and the Vital Scientific Flexor Junior Analyzer.

ELITech Clinical Systems ELITROL I is a multi-parametric control serum for *in vitro* diagnostic use in accuracy control of quantitative ELITech Clinical Systems methods on the Vital Scientific Selectra Junior Analyzer and the Vital Scientific Flexor Junior Analyzer.

ELITech Clinical Systems ELITROL II is a multi-parametric control serum for *in vitro*

diagnostic use in accuracy control of quantitative ELITech Clinical Systems methods on the Vital Scientific Selectra Junior Analyzer and the Vital Scientific Flexor Junior Analyzer.

3. Special conditions for use statement(s):

For *in vitro* diagnostic use only; this assay is not intended for point of care settings.

The labeling contains a statement that all human source material was tested by FDA-approved methods and found to be non-reactive for the presence of HBsAg, HCV and antibody to HIV 1/2.

4. Special instrument requirements:

All performance was evaluated on the Vital Scientific Selectra Junior Analyzer which is also trademarked as the Vital Scientific Flexor Junior Analyzer (k973628)

I. Device Description:

1. ELITech Clinical Systems CHOLESTEROL HDL SL 2G Kit Contents:

- a. Reagent R1 – 4 vials of liquid ready to use – 21 mL each vial
 - i. Good's Buffer
 - ii. Cholesterol Oxidase (CO bacterial)
 - iii. Peroxidase (POD horseradish)
 - iv. Ascorbate Oxidase (bacterial)
 - v. N,N-bis(4-sulphobutyl)-*m*-toluidine-disodium (DBSmT)
 - vi. Accelerator and preservative
- b. Reagent R2 – 4 vials of liquid ready to use – 7 mL each vial
 - i. Good's Buffer
 - ii. Cholesterol Esterase (CHE bacterial)
 - iii. 4-Amino-Antipyrine (4-AA)
 - iv. Detergent and Preservative

2. ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR Kit Contents:

- a. 4 vials of Lyophilized human serum based calibrator – makes 1 mL per vial
 - i. Lipoprotein from the various lipoprotein classes including high density lipoprotein
 - ii. Sodium Azide Preservative

3. ELITech Clinical Systems CHOLESTEROL LDL SL 2G Kit Contents:

- a. Reagent R1 – 4 vials of liquid ready to use – 21 mL each vial
 - i. MES Buffer (2-(N-morpholino)ethanesulfonic acid)
 - ii. Detergent 1
 - iii. Cholesterol Esterase (CHE bacterial)

- iv. Cholesterol Oxidase (CO bacterial)
 - v. Peroxidase (POD horseradish)
 - vi. 4-Amino-Antipyrine (4-AA)
 - vii. Ascorbate Oxidase (vegetal)
 - b. Reagent R2 – 4 vials of liquid ready to use – 7 mL each vial
 - i. MES Buffer
 - ii. Detergent 2
 - iii. N,N-bis(4-sulphobutyl)-*m*-toluidine-disodium (DBSmT)
- 4. ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR Kit Contents:
 - a. 4 vials of Lyophilized human serum based calibrator – makes 1 mL per vial
 - i. Lipoprotein from the various lipoprotein classes including low density lipoprotein
 - ii. Sodium Azide Preservative
- 5. ELITech Clinical Systems ELITROL I and ELITROL II
 - a. 10 vials of Lyophilized human serum based control – makes 5 mL per vial
 - i. Lipoprotein from the various lipoprotein classes
 - ii. Preservative

J. Substantial Equivalence Information:

1. Predicate device name(s):

- 1. HORIBA ABX PENTRA HDL Direct CP
- 2. Genzyme Ultra N-Geneous CHOLESTEROL HDL Calibrator
- 3. HORIBA ABX PENTRA LDL Direct CP
- 4. Genzyme Ultra N-Geneous CHOLESTEROL LDL Calibrator
- 5. Roche Precinorm U / Precipath U

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

- 1. k060854
- 2. k021316
- 3. k060854
- 4. k971573
- 5. k041227

3. Comparison with predicate:

Items	ELITech Clinical Systems CHOLESTEROL HDL SL 2G (Candidate Device)	ABX PENTRA HDL Direct CP (Predicate Device)
Similarity		
Intended Use	Same	For the <i>in vitro</i> determination of High Density Lipoprotein Cholesterol (HDL-C) in human serum or plasma by colorimetry.
Test Principle	Same	Enzymatic colorimetric test using accelerator selective detergent
Reagent Composition	Same	<u>Reagent R1:</u> Good's Buffer Cholesterol Oxidase Peroxidase N,N-bis(4-sulphobutyl)- <i>m</i> -toluidine-disodium Accelerator Preservative <u>Reagent R2:</u> Good's Buffer Cholesterol Esterase 4-Amino-Antipyrine Detergent Preservative
Reagent Form	Same	Liquid – ready to use
Sample Type	Same	Serum and Li-Heparin Plasma
Reagent Storage	Same	2-8°C away from light until expiration date
Expected Values	Same	<u>According to NCEP:</u> High Risk: < 40 mg/dL Low Risk: ≥60 mg/dL
Difference		
Reagent Composition	<u>Reagent R1:</u> Ascorbate oxidase	<u>Reagent R2:</u> Restrainer Ascorbic Acid Oxidase
Instrument	SELECTRA JUNIOR	ABX PENTRA 400
Measuring Range	5 – 105 mg/dL	5.4 – 151.9 mg/dL
Limit of Detection	0.7 mg/dL	1.16 mg/dL
Limit of Quantitation	5.0 mg/dL	
Precision	<u>Within-run % CV:</u> Level 31 mg/dL = 1.4% Level 56 mg/dL = 0.7% Level 87 mg/dL = 1.4% <u>Total % CV:</u> Level 31 mg/dL = 3.0% Level 56 mg/dL = 2.8% Level 87 mg/dL = 3.3%	<u>Within-run % CV:</u> Level 27.94 mg/dL = 1.32% Level 35.82 mg/dL = 1.29% Level 48.59 mg/dL = 1.91% Level 81.72 mg/dL = 0.79% Level 97.39 mg/dL = 0.62% <u>Total % CV:</u> Level 35.85 mg/dL = 2.88% Level 47.07 mg/dL = 3.52% Level 80.16 mg/dL = 2.69% Level 80.35 mg/dL = 3.06%
Method Comparison with	$y=1.09x-2.5$ mg/dL $r^2=0.973$	$y=0.91x+1.98$ mg/dL $r^2=0.9768$

Predicate	range: 5 – 105 mg/dL	range: 5.4 – 151.9 mg/dL
Limitations	<u>No Significant Interference From:</u> Unconjugated bilirubin (<30 mg/dL) Conjugated bilirubin (<29.5 mg/dL) Hemoglobin (<500 mg/dL) Turbidity: Negative bias from 439 mg/dL triglycerides equivalent	<u>No Significant Interference From:</u> Total bilirubin (<11.7 mg/dL) Direct Bilirubin (<28.1 mg/dL) Hemoglobin (<479 mg/dL) Triglycerides (<612.5 mg/dL)
On-Board Stability	Refrigerated Area: 28 days	Refrigerated Area: 31 days

Items	ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR (Candidate Device)	Genzyme Ultra N-Geneous CHOLESTEROL HDL Calibrator (Predicate Device)
Similarity		
Intended Use	Same	For the calibration of the associated HDL Cholesterol assay
Format	Same	Lyophilized calibrator based on human serum containing various lipoproteins including high density lipoprotein – contains sodium azide as a preservative
Level	Same	Single level
Handling	Same	Carefully open the vial to avoid loss of lyophilizate, and reconstitute with 1 mL deionized water. Allow the closed vial to sit for 20 minutes, and swirl gently to avoid formation of foam. Do not shake.
Stability	Same	<u>Lyophilized:</u> Store at 2-8°C protected from light until expiry date <u>Post-Reconstitution:</u> 14 days at 2-8 °C 4 weeks at <80 °C (freeze only once)

Items	ELITech Clinical Systems CHOLESTEROL LDL SL 2G (Candidate Device)	ABX PENTRA LDL Direct CP (Predicate Device)
Similarity		
Intended Use	Same	For the <i>in vitro</i> determination of Low Density Lipoprotein Cholesterol (LDL-C) in human serum or plasma by colorimetry.
Test Principle	Same	Enzymatic colorimetric test using selective detergent
Reagent Composition	Same	<u>Reagent R1:</u> MES Buffer Detergent 1

		Cholesterol Esterase Cholesterol Oxidase Peroxidase 4-Amino-Antipyrine Ascorbate Oxidase Preservative <u>Reagent R2:</u> MES Buffer Detergent 2 N,N-bis(4-sulphobutyl)- <i>m</i> -toluidine- disodium Preservative
Reagent Form	Same	Liquid – ready to use
Sample Type	Same	Serum and Li-Heparin Plasma
Reagent Storage	Same	2-8°C away from light until expiration date
Expected Values	Same	According to NCEP Risk Classifications: Optimal: < 100 mg/dL Near Optimal: 100-129 mg/dL Borderline High: 130-159 mg/dL High: 160-189 mg/dL Very High: ≥190 mg/dL
Difference		
Instrument	SELECTRA JUNIOR	ABX PENTRA 400
Measuring Range	15 – 380 mg/dL	1.35 – 369.39 mg/dL
Limit of Detection	0.3 mg/dL	1.55 mg.dL
Limit of Quantitation	10.0 mg/dL	
Precision	<u>Within-run % CV:</u> Level 108 mg/dL = 1.4% Level 122 mg/dL = 1.3% Level 162 mg/dL = 2.0% <u>Total % CV:</u> Level 108 mg/dL = 2.6% Level 122 mg/dL = 2.7% Level 162 mg/dL = 4.0%	<u>Within-run % CV:</u> Level 61.26 mg/dL = 1.01% Level 75.08 mg/dL = 2.82% Level 111.26 mg/dL = 0.91% Level 141.16 mg/dL = 1.00% Level 191.16 mg/dL = 0.63% <u>Total % CV:</u> Level 60.64 mg/dL = 5.59% Level 74.27 mg/dL = 6.39% Level 156.58 mg/dL = 3.94% Level 191.62 mg/dL = 4.04%
Method Comparison with Predicate	$y=0.999x-0.5$ mg/dL $r^2=0.993$ range: 16 – 378 mg/dL	$y=0.96x-0.21$ mg/dL $r^2=0.9963$ range: 1.35 – 369.39 mg/dL
Limitations	<u>No Significant Interference From:</u> Unconjugated bilirubin (<30 mg/dL) Conjugated bilirubin (<29.5 mg/dL) Hemoglobin (<500 mg/dL) Turbidity: Negative bias from 614 mg/dL triglycerides equivalent	<u>No Significant Interference From:</u> Total bilirubin (<8.19 mg/dL) Direct Bilirubin (<5.63 mg/dL) Hemoglobin (<460 mg/dL) Triglycerides (<613 mg/dL)
Calibration	28 days	14 days

Frequency		
On-Board Stability	Refrigerated Area: 28 days	Refrigerated Area: 97 days

Items	ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR (Candidate Device)	Genzyme Ultra N-Geneous CHOLESTEROL LDL Calibrator (Predicate Device)
Similarity		
Intended Use	Same	For the calibration of the associated LDL Cholesterol assay
Format	Same	Lyophilized calibrator based on human serum containing various lipoproteins including low density lipoprotein – contains sodium azide as a preservative
Level	Same	Single level
Handling	Same	Carefully open the vial to avoid loss of lyophilizate, and reconstitute with 1 mL deionized water. Allow the closed vial to sit for 5 minutes, and swirl gently to avoid formation of foam. Do not shake.
Stability	Same	<u>Lyophilized:</u> Store at 2-8°C protected from light until expiry date <u>Post-Reconstitution:</u> 14 days at 2-8 °C 4 weeks at <80 °C (freeze only once)

Items	ELITech Clinical Systems ELITROL I and ELITROL II (Candidate Device)	Roche Precinorm U / Precipath U (Predicate Device)
Similarity		
Intended Use	Same	For the <i>in vitro</i> diagnostic use in the quality control for the quantitative determination of HDL and LDL Cholesterol by the respective method.
Format	Same	Lyophilized human sera with constituents added as required to obtain desired component levels
Levels	Same	Two levels
Handling	Same	Carefully open the vial to avoid loss of lyophilizate, and reconstitute with 5 mL deionized water. Dissolve lyophilizate with occasional gentle swirling for 30 minutes, and avoid the formation of foam.
Stability	Same	<u>Lyophilized:</u> Store at 2-8°C protected from light until expiry date <u>Post-Reconstitution:</u>

		12 hours at 15-25 °C 5 days at 2-8 °C 4 weeks at -25 to -15 °C (freeze only once)
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K. Standard/Guidance Document Referenced (if applicable):

- CLSI Guideline EP05-A2: Evaluation of Precision Performance of Qualitative Measurement Methods
- CLSI Guideline EP06-A: Evaluation of the Linearity of Qualitative Measurement Methods
- CLSI Guideline EP07-A2: Interference Testing in Clinical Chemistry
- CLSI Guideline EP09-A2: Method Comparison and Bias Estimation Using Patient Samples
- CLSI Guideline EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation
- CEN 13640: Stability Testing of In Vitro Diagnostic Reagents

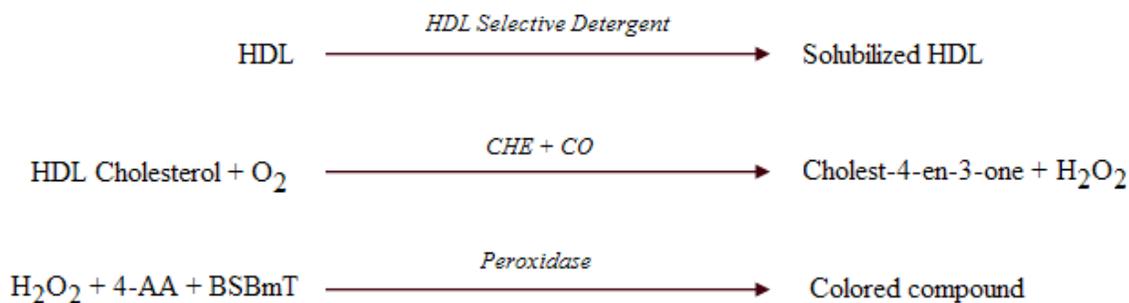
L. Test Principle:

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

An enzymatic colorimetric determination of HDL cholesterol based on accelerator selective detergent. First, the patient sample is mixed with reagent R1 containing a selective accelerator to deactivate all cholesterol of non-HDL lipoproteins (LDL, VLDL & chylomicrons):



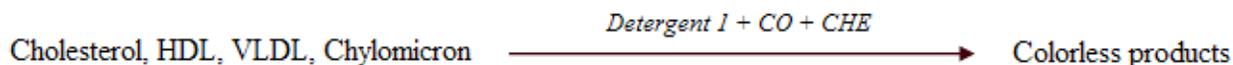
Second, reagent R2 is added to solubilize and enzymatically measure HDL via a color formation with peroxidase:



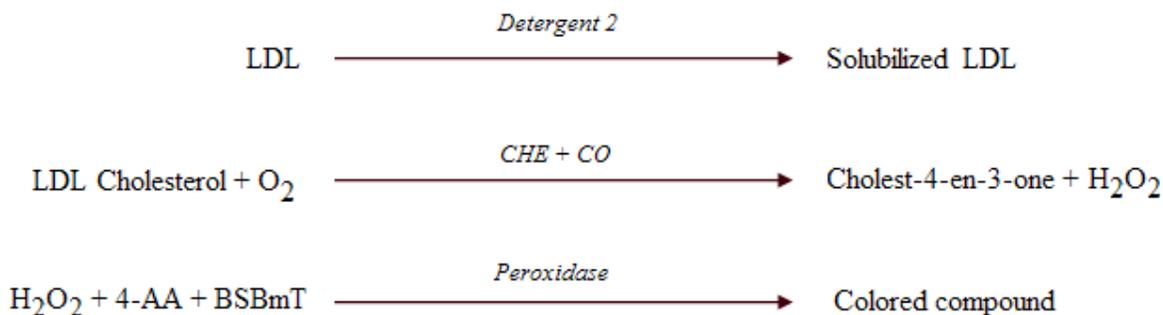
ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

An enzymatic colorimetric determination of LDL cholesterol based on selective detergent.

First, the sample is mixed with reagent R1 to solubilize non-LDL lipoproteins and eliminate released cholesterol:



Second, reagent R2 is added to solubilize LDL and measure it by color formation:



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Precision was evaluated following guideline EP5-A2. Two replicates each of 3 control samples at clinically relevant decision levels were tested twice a day on 20 separate days, yielding 80 replicates total over 40 runs. Control samples included one diluted (all dilutions for performance testing was done with saline) human sera pool sample, one human sera pool sample, and one spiked human sera pool sample. The results are presented in the table below:

Precision Results:

Sample	Units = mg/dL							No. Observ.	No. Days
	Mean HDL	Within-run		Between-day		Total			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
Low Sample	31	0.4	1.4%	0.7	2.3%	0.9	3.0%	80	20
Medium Sample	56	0.4	0.7%	1.1	2.0%	1.6	2.8%	80	20
High Sample	87	1.2	1.4%	1.6	1.8%	2.8	3.3%	80	20

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Precision was evaluated following guideline EP5-A2. Two replicates each of 3 control

samples at clinically relevant decision levels were tested twice a day on 20 separate days, yielding 80 replicates total over 40 runs. Control samples included one low sample of liquicheck lipid 1, one normal human sera pool sample, and one spiked human sera pool sample. The results are presented in the table below:

Precision Results:

Sample	Units = mg/dL							No. Observ.	No. Days
	Mean HDL	Within-run		Between-day		Total			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
Low Sample	108	1.5	1.4%	1.6	1.4%	2.8	2.6%	80	20
Medium Sample	122	1.5	1.3%	1.7	1.4%	3.2	2.7%	80	20
High Sample	162	3.2	2.0%	0.0	0.0%	6.4	4.0%	80	20

b. Linearity/assay reportable range:

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Study Protocol:

Linearity was evaluated following CLSI guideline EP6-A. Serum pools were used for the studies. High spiked pool samples were diluted using low pool samples (serum diluted with saline) to give a total of 8 sample dilutions, ranging from 5 mg/dL to 110 mg/dL. Statistical evaluation gave the following results:

Serum Linearity Study:

$$y = 1.05x - 2$$

$$r = 0.9989$$

Based on the linearity results, the sponsor claimed that the assay is linear from 5 mg/dL to 105 mg/dL.

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Study Protocol:

Linearity was evaluated following CLSI guideline EP6-A. Serum pools were used for the studies. High spiked pool samples were diluted using low pool samples (serum diluted with saline) to give a total of 11 sample dilutions, ranging from 15 mg/dL to 380 mg/dL. Statistical evaluation gave the following results:

Serum Linearity Study:

$$y = 1.031x - 5$$

$$r = 0.9994$$

Based on the linearity results, the sponsor claimed that the assay is linear from 15 mg/dL to 380 mg/dL.

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

Traceability:

The ELITech Clinical Systems CHOLESTEROL HDL 2G CALIBRATOR, the ELITech Clinical Systems CHOLESTEROL LDL 2G CALIBRATOR, and the ELITech Clinical Systems ELITROL I and ELITROL II are traceable to the reference method recommended by the CDC. These calibrators are all reviewed under 510(k) numbers k021316, k971573, and k093883 respectively.

Stability:

Real-time testing as well as on-board, shelf life and post-reconstitution stability studies were conducted. The stability study protocols and the sponsor defined acceptance criteria have been reviewed and found to be acceptable. The study results support the stability claims summarized in the below table.

Stability Results:

Item	Storage Conditions		Claimed Stability
HDL Reagent Packs	Close-Vial	2-8°C	24 months
	Open-Vial	On system	28 days
HDL Calibrator	Close-Vial	2-8°C	24 months
	Open-Reconstituted	2-8°C	14 days
	Open-Reconstituted	≤ -80°C	4 weeks
LDL Reagent Packs	Close-Vial	2-8°C	24 months
	Open-Vial	On system	28 days
LDL Calibrator	Close-Vial	2-8°C	24 months
	Open-Reconstituted	2-8°C	14 days
	Open-Reconstituted	≤ -80°C	4 weeks
Controls	Close-Vial	2-8°C	24 months
	Open-Reconstituted	15-25°C	12 hours
	Open-Reconstituted	2-8°C	5 days
	Open-Reconstituted	-25 to -15°C	4 weeks

Calibration Interval:

ELITech Clinical Systems CHOLESTEROL HDL 2G and LDL 2G CALIBRATORS:

Stability across a 28 day calibration interval was assessed by calculating the percentage bias of the precision samples on each day from the result obtained for that precision

samples from the calibration on the first day. The results support the product claim of a 28-day calibration interval.

Value Assignment:

ELITech Clinical Systems CHOLESTEROL HDL 2G and LDL 2G CALIBRATORS:

Value assignment of all calibrators is obtained by assaying the new calibrator sets as unknowns, run in triplicate on one machine. The mean is calculated based upon comparison with an already approved calibrator lot. Acceptance criteria state that the new calibrators must fall within $\pm 10\%$ of the target values.

ELITech Clinical Systems ELITROL I and ELITROL II

Value assignment of controls is obtained by assaying 3 vials of reconstituted controls of the same lot, run in triplicate on one machine. The mean is calculated and compared to the certificate of analysis from the manufacturing company. Acceptance criteria state that the controls must fall within $\pm 15\%$ of the target values listed in the certificate of analysis.

The ELITech Clinical Systems CHOLESTEROL HDL SL 2G and CHOLESTEROL LDL SL 2G assays have not been tested or certified by the Cholesterol Reference Method Laboratory Network (CRMLN).

d. Detection limit:

Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined following guideline EP17-A.

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Study Protocol:

For LoB determination, 60 replicates of blank samples were measured on one day, using one analyzer and one reagent lot – giving 60 determinations in total.

For LoD determination, four diluted sample pools were prepared from four different patient samples pools and diluted with saline to obtain a concentration close to four times the calculated LoB. Each of the sample pools was measured 15 times in one run, using one instrument and one reagent lot. As the resultant data was not Gaussian, the LoD was calculated as $LoB + D_{S,\beta}$ (where $D_{S,\beta}$ is determined by calculating the median minus the 5th percentile in the low concentration sample distribution).

For LoQ determination, four sample pools were prepared from four different patient samples pools and diluted with saline to obtain a concentration close to the expected LoQ. Each of the sample pools was measured 15 times in one run, using one instrument and

one reagent lot. By calculating the total error interval ($= \text{Bias} \pm 2\text{SD}$) with a sponsor defined acceptance criterion of $\leq 15.8\%$ total error, the LoQ was determined and was acceptable.

Result Summary HDL:

Based on the study result, the following detection limit claims were made:

LoB	LoD	LoQ
0.3 mg/dL	0.7 mg/dL	5 mg/dL

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Study Protocol:

For LoB determination, 60 replicates of blank samples were measured on one day, using one analyzer and one reagent lot – giving 60 determinations in total.

For LoD determination, four diluted sample pools were prepared from four different patient samples pools and diluted with saline to obtain a concentration close to four times the calculated LoB. Each of the sample pools was measured 15 times in one run, using one instrument and one reagent lot. As the resultant data was not Gaussian, the LoD was calculated as $\text{LoB} + D_{S,\beta}$ (where $D_{S,\beta}$ is determined by calculating the median minus the 5th percentile in the low concentration sample distribution).

For LoQ determination, four sample pools were prepared from four different patient samples pools and diluted with saline to obtain a concentration close to the expected LoQ. Each of the sample pools was measured 15 times in one run, using one instrument and one reagent lot. By calculating the total error interval ($= \text{Bias} \pm 2\text{SD}$) with a sponsor defined acceptance criterion of $\leq 12\%$ total error, the LoQ was determined and was acceptable.

Result Summary LDL:

Based on the study result, the following detection limit claims were made:

LoB	LoD	LoQ
0.1 mg/dL	0.3 mg/dL	10 mg/dL

e. Analytical specificity:

- Interference

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Study Protocol:

The sponsor evaluated the effect of the interfering substances using two patient serum pools with endogenous HDL at 31 mg/dL and 54 mg/dL. For each potential interfering substance, between 5 and 9 different concentrations were spiked with the test substance up to the maximum level shown below. The sponsor defined no significant interference as $\pm \leq 10\%$. The HDL results (mean of triplicates) of the paired pools were compared and % difference was calculated and evaluated for interference determination.

Result Summary:

Based on the sponsor-defined interference limit of $\pm 10\%$, the following claims were made:

- ❖ The below compounds at the indicated concentration do not cause significant interference with the assay.

Compound	Concentration up to
Bilirubin (unconjugated)	30 mg/dL
Bilirubin (conjugated)	29.5 mg/dL
Hemoglobin	500 mg/dL
Triglycerides (Intralipid)	439 mg/dL

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Study Protocol:

The sponsor evaluated the effect of the interfering substances using two patient serum pools with endogenous LDL at 100 mg/dL and 160 mg/dL. For each potential interfering substance, between 5 and 9 different concentrations were spiked with the test substance up to the maximum level shown below. The sponsor defined no significant interference as $\pm \leq 10\%$. The LDL results (mean of triplicates) of the paired pools were compared and % difference was calculated and evaluated for interference determination.

Result Summary:

Based on the sponsor-defined interference limit of $\pm 10\%$, the following claims were made:

- ❖ The below compounds at the indicated concentration do not cause significant interference with the assay.

Compound	Concentration up to
Bilirubin (unconjugated)	30 mg/dL
Bilirubin (conjugated)	29.5 mg/dL
Hemoglobin	500 mg/dL
Triglycerides (Intralipid)	614 mg/dL
Ascorbic Acid	20 mg/dL

The package insert for each the HDL and LDL assays contains a statement that other compounds may interfere and users should refer to the following literature references:

- Young, D. S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
- Young, D.S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).
- Berth, M. & Delanghe, J. *Protein precipitation as a possible important pitfall in the clinical chemistry analysis of blood samples containing monoclonal*

immunoglobulins: 2 case reports and a review of literature, Acta Clin Belg., (2004), 59, 263.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Study Protocol:

A total of 88 patient serum samples (3 spiked) from an independent clinical laboratory and a hospital laboratory were used in the method comparison studies. Samples were assayed in duplicate and ranged from 5 mg/dL to 94 mg/dL

Result Summary:

Linear Regression analysis yielded the equation $y = 1.09x - 2.5$, with an r value of 0.986.

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Study Protocol:

A total of 100 patient serum samples (7 spiked and 3 diluted) from an independent clinical laboratory and a hospital laboratory were used in the method comparison studies. Samples were assayed in duplicate and ranged from 16 mg/dL to 378 mg/dL. Regression analysis was performed between the candidate system and the predicate ABX Pentra system.

Result Summary:

Linear Regression analysis yielded the equation $y = 0.999x - 0.5$, with an r value of 0.997.

b. Matrix comparison:

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

Study Protocol:

The matrix effect on serum and Li-Heparin plasma samples was evaluated. 32 matched patient samples were enrolled in the study. To cover the entire measuring range of the assay, three of the samples were spiked and one sample was diluted. Samples ranged from 6 to 94 mg/dL. Differences in HDL values (mean of duplicate determinations) between serum and plasma was evaluated using a Bias plot and correlation graph.

Result Summary:

Linear Regression analysis yielded the equation $y = 0.952x + 0.74$, with an r value of 0.990.

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

Study Protocol:

The matrix effect on serum and Li-Heparin plasma samples was evaluated. 40 matched patient samples were enrolled in the study. To cover the entire measuring range of the assay, three of the samples were spiked and one sample was diluted. Samples ranged from 15 to 365 mg/dL. Differences in LDL values (mean of duplicate determinations) between serum and plasma was evaluated using a Bias plot and correlation graph.

Result Summary:

Linear Regression analysis yielded the equation $y = 0.987x - 2$, with an r value of 0.997.

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:

ELITech Clinical Systems CHOLESTEROL HDL SL 2G:

The reference intervals listed were taken from literature*.

Cardiovascular Risk	Conventional units	S.I. units
Low	≥ 60 mg/dL	≥ 1.55 mmol/L
High	< 40 mg/dL	< 1.03 mmol/L

*Expert Panel on Detection, *Evaluation and Treatment of High Cholesterol in Adults (Adult Treatment Panel III)*, May (2001).

NIH Publication No. 01 3305, *ATP III Guidelines At-A-Glance*, Quick Desk Reference, May (2001).
NIH Publication No. 01 3670, Third Report of National Cholesterol Education Program (NCEP).

The package insert includes precautionary language that each laboratory should establish its own reference intervals based upon its patient population.

ELITech Clinical Systems CHOLESTEROL LDL SL 2G:

The reference intervals listed were taken from literature*.

Classification	Conventional units	S.I. units
Optimal	< 100 mg/dL	< 1.00 mmol/L
Near Optimal	100 – 129 mg/dL	1.00 – 1.29 mmol/L
Borderline High	130 – 159 mg/dL	1.30 – 1.59 mmol/L
High	160 – 189 mg/dL	1.60 – 1.89 mmol/L
Very High	≥ 190 mg/dL	≥ 4.91 mmol/L

*The reference Interval for LDLC is based on the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); Executive Summary. NIH Publication No. 01-3670, National Institutes of Health. Bethesda. Maryland: May 2001.

The package insert includes precautionary language that each laboratory should establish its own reference intervals based upon its patient population.

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.