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

A. 510(k) Number:

k110830

B. Purpose for Submission:

New device

C. Measurand:

Albumin, Calcium

D. Type of Test:

Quantitative, colorimetric chemistry tests

E. Applicant:

Seppim S.A.S.

F. Proprietary and Established Names:

ELITech Clinical Systems Calcium Arsenazo
ELITech Clinical Systems Albumin
ELITech Clinical Systems ELICAL 2
ELITech Clinical Systems ELITROL I
ELITech Clinical Systems ELITROL II

G. Regulatory Information:

Measurand	Regulation Section	Classification	Product Code	Panel
Albumin	21CFR862.1035	II	CIX- Bromocresol green dye-binding, albumin	(75) Clinical Chemistry
Calcium	21CFR862.1145	II	CJY – Azo dye, calcium	(75) Clinical Chemistry
Calibrator	21CFR862.1150	II	JIX- Calibrator, multi-analyte mixture	(75) Clinical Chemistry
Control	21CFR862.1660	I, Reserved	JJY – Multi-Analyte Controls	(75) Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   ELITech Clinical Systems Albumin
   ELITech Clinical Systems Albumin is intended for the quantitative in vitro diagnostic determination of albumin in human serum and plasma on ELITech Clinical Systems Selectra analyzers. It is not intended for use in Point of Care settings.

   Albumin measurements are used in the diagnosis and treatment of numerous diseases involving primarily the liver or kidneys.

   ELITech Clinical Systems Calcium Arsenazo
   ELITech Clinical Systems Calcium Arsenazo is intended for the quantitative in vitro diagnostic determination of total calcium in human serum and plasma on ELITech Clinical Systems Selectra analyzers. It is not intended for use in Point of Care settings.

   Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

ELITech Clinical Systems ELICAL 2
ELITech Clinical Systems ELICAL 2 is a multi-parametric calibrator for in vitro diagnostic use in the calibration of quantitative ELITech Clinical Systems methods on ELITech Clinical Systems Selectra analyzers.

ELITech Clinical Systems ELITRIOL I and ELITRIOL II
ELITech Clinical Systems ELITRIOL I and ELITRIOL II are multi-parametric control sera for in vitro diagnostic use in quality control of quantitative ELITech Clinical Systems methods on ELITech Clinical Systems Selectra analyzers.

3. Special conditions for use statement(s):

   For *in vitro* diagnostic use only. For prescription use only

4. Special instrument requirements:

   For use with the ELITech Clinical Systems Selectra ProM analyzer

I. Device Description:

The ELITech Clinical Systems Calcium Arsenazo and ELITech Clinical Systems Albumin kit reagents are one reagent systems. Reagents are supplied in liquid ready-to-use forms. Each kit is composed of 12 x 20 mL vials of reagent. The calcium reagent contains MES buffer (100 mM) and arsenazo III (200 µM). The albumin reagent contains succinate buffer (87 mM), bromocresol green (0.2 mM), and non-ionic surfactant brij 35 (7.35 mL/L).

ELITech Clinical Systems ELICAL2 is a lyophilized calibrator based on human serum containing constituents to ensure optimal calibration. ELICAL 2 is prepared exclusively from the blood of donors tested individually and found to be negative for HbsAg and to the antibodies to HCV and HIV according to FDA-approved methods.

ELITROL I and ELITROL II are two level quality control products consisting of a lyophilized human serum containing constituents at desired levels. ELITROL I and ELITROL II are prepared exclusively from the blood of donors tested individually and found to be negative for HBsAg and to antibodies to HCV and HIV according to FDA-approved methods.

Substantial Equivalence Information:

1. Predicate Device Name(s):
   Stanbio Calcium LiquiColor (Arsenazo III)
   Roche Diagnostics Albumin Gen.2
   Roche Diagnostics Calibrator for Automated Systems
   Roche Diagnsotics Precinorm Universal and Precipath Universal Control Sera

2. Predicate 510(k) number(s):
   k921625, k063744, k033501, k041227

3. Comparison with predicate:

Similarities and Differences for Albumin		
Item	Candidate Device ELITech Clinical Systems Albumin	Predicate Device (k063744) Roche Diagnostics Albumin Gen.2
Intended Use	Intended for the quantitative in vitro diagnostic determination of albumin in human serum and plasma.	Same
Indications For Use	Albumin measurements are used in the diagnosis and treatment of numerous diseases involving primarily the liver or kidneys.	Same
Specimen Type	Human serum, plasma	Same
Assay Type	Liquid ready-for-use	Same
Assay Principle	Colorimetric	Same
Analytical Range	1.6 – 6.0 g/dL	0.2 – 6.0 g/dL
Reagent Storage	2-25°C, stable until expiration date on label	15-25°C, stable until expiration date on label
Stability (on board)	28 days	4 weeks
Instrument	Selectra ProM Analyzer	Cobas c111 Analyzer

Similarities and Differences for Calcium		
Item	Candidate Device ELITech Clinical Systems Calcium Arsenazo	Predicate Device (k921625) Stanbio Calcium LiquiColor Arsenazo III
Intended Use	Intended for the quantitative in vitro diagnostic determination of total calcium in human serum and plasma.	Same

Indications For Use	Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).	Same
Specimen Type	Human serum, plasma	Same
Assay Type	Liquid ready-for-use	Same
Assay Principle	Colorimetric	Same
Analytical Range	5.0 – 15.0 mg/dL	0 – 15.0 mg/dL
Reagent Storage	2-8°C, stable until expiration date on label	2-30°C, stable until expiration date on label
Stability (on board)	28 days	30 days
Instrument	Selectra ProM Analyzer	Sirrus Chemistry Analyzer

Similarities and Differences for Calibrator (ELICAL 2)		
Item	Candidate Device ELITech Clinical Systems ELICAL 2	Predicate Device (k033501) Roche Diagnostics Calibrator for Automated Systems
Intended Use/Indications for Use	For in vitro diagnostic use in the calibration of quantitative methods	Same
Format	Lyophilized calibrator based on human sera	Same
Levels	One	Same
Stability	Lyophilized: 2 to 8°C, stable until expiration date on label Reconstituted: 15 to 25°C, 8 hours 2 to 8 °C, 2 days -25 to -15°C, 4 weeks	Same

Similarities and Differences for Controls (ELITROL I and II)		
Item	Candidate Device ELITech Clinical Systems ELITROL I and ELITROL II	Predicate Device (k041227) Roche Diagnsotics Precinorm Universal and Precipath Universal Control Sera
Intended Use/Indications for Use	For in vitro diagnostic use in quality control of quantitative methods	Same
Format	Lyophilized controls based on human sera	Same
Levels	Two (ELITROL I and ELITROL II)	Same
Stability	Lyophilized: 2 to 8°C, stable until expiration date on label Reconstituted: 15 to 25°C, 12 hours 2 to 8 °C, 5 days -25 to -15°C, 4 weeks	Same

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

- CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices – Second Edition*
- CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples – Second Edition*
- CLSI Guideline, EP6-A *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*
- CLSI Guideline, EP7-A2 *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*
- CLSI Guideline, EP17-A *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline*
- FR EN 13640:2002 *Stability Testing of In Vitro Diagnostic Reagents*
- *In Vitro Diagnostics Devices: Guidance for the preparation of 510(k) submissions (1977)*
- *Guidance for Industry and FDA Staff: "Format for Traditional and Abbreviated 510(k)s" (2005)*
- *Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use: Guidance for Industry and FDA Staff (2004)*

L. Test Principle:

ELITech Clinical Systems Albumin
This method involves the binding of albumin with bromocresol green. Bromocresol green forms a complex with albumin at pH 4.20. The color intensity at 620 nm is directly proportional to the albumin concentration in the sample.

ELITech Clinical Systems Calcium Arsenazo
This method utilizes Arsenazo III, which has a high affinity for calcium at neutral pH. Arsenazo III forms in neutral medium a blue complex with calcium. The color intensity at 600 nm in directly proportional to the total calcium concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Serum -Within run and total precision studies were performed according to CLSI EP5-A2 for albumin and calcium. Studies were performed by conducting two runs per day, two measures per run, for 3 levels of samples, on 2 Selectra ProM instruments for 20 operating days. For albumin, data from level 1 is from a diluted serum sample, level 2 is from a natural human serum pool sample, and level 3 is from a spiked human serum pool sample. For calcium, data from level 1 is from a control serum sample, level 2 is from a natural human serum pool sample, and level 3 is from a spiked human serum pool sample. Results are presented in the tables below.

Albumin

	Level 1	Level 2	Level 3
Concentration Levels (g/dL)	2.50	3.50	5.00
No. of Samples	80	80	80
No. of Replicates	2	2	2
Mean	2.54	3.53	4.98
Total SD	0.06	0.08	0.10
Total %CV	2.3	2.1	2.1
Within-Run SD	0.02	0.02	0.04
Within-Run %CV	0.9	0.5	0.8

Calcium

	Level 1	Level 2	Level 3
Concentration Levels (mg/dL)	8.00	10.00	12.00
No. of Samples	80	80	80
No. of Replicates	2	2	2
Mean	8.75	9.68	11.97
Total SD	0.17	0.19	0.22
Total %CV	1.9	1.9	1.9
Within-Run SD	0.11	0.09	0.08
Within-Run %CV	1.3	0.9	0.7

b. Linearity/assay reportable range:

Serum-Linearity was evaluated for albumin and calcium according to CLSI EP6-A by comparing observed versus expected values for 11 equally-spaced serum samples. Samples were prepared from high and low analyte concentration serum pools. Each sample was evaluated in triplicate on the Selectra ProM instrument. Linear regression results from these studies are found in the table below.

	Slope	Intercept	R^2	Standard Error	Concentration Ranges tested
ALB	0.9648	0.1082	0.9976	0.08	1.55 – 6.08 g/dL
Ca	1.0235	-0.1865	0.9993	0.10	4.96 – 15.39 mg/dL

The results of the study support the sponsor's claims that albumin assay is linear across the measuring range of 1.6 – 6.0 g/dL and the calcium assay is linear across the measuring range of 5.0 – 15.0 mg/dL.

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

Traceability

The sponsor claims traceability of albumin and calcium used in the ELICAL 2 calibrator, ELITROL I, and ELITRIOL II to reference materials, ERM-DA 470 and SRM 909b, respectively.

Value Assignment

The ELICAL 2 calibrator solution and the ELITROL I and ELITROL II

control solutions are tested against predetermined values on the Selectra ProM analyzer using the albumin and calcium reagents. Value assignment for the ELICAL 2 calibrator solution was performed by quadruplicate runs on the Selectra ProM analyzer, using 2 reagent lots, and 3 test vials per lot. Value assignment for the ELITROL I and ELITRIOL II control solutions was performed by triplicate runs on the Selectra ProM analyzer, using 2 reagent lots, and 3 test vials per lot. The mean analyte value is calculated and a target value is assigned. The labeling states that obtained control solution values should fall within the specified range provided on lot-specific value sheets and that laboratories should establish appropriate quality control procedures when using this product for its intended use. The labeling also states that laboratories should recalibrate when reagents lots change, when quality control results fall out of range, and after a maintenance operation.

Stability

Calibrator material is purchased from a commercial vendor (previously cleared under k033501). The sponsor claimed the following for stability: ELICAL 2 is stable until the expiration date printed on the label when stored at 2-8˚C prior to reconstitution. After reconstitution the stability is 8 hours when stored at 15-25˚C, 2 days at 2-8˚C or 4 weeks (when frozen once) at -25˚and -15˚C.

Control material is purchased from a commercial vendor (previously cleared under k041227). The sponsor claimed the following for stability: Before reconstitution, the shelf-life of the ELITech Clinical Systems Elitrol I and Elitrol II is 30 months at 2-8˚C. After reconstitution the stability is 12 hours when stored at 15-25˚C, 5 days when stored at 2-8˚C or 4 weeks (when frozen once) at -25˚ and -15˚ C.

d. Detection limit:

Serum-Limit of blank (LoB), limit of detection (LoD), and limit of quantification (LoQ) were determined according to CLSI EP17-A with the Selectra ProM instrument for calcium and albumin. Testing was conducted over multiple days, with one run across two instruments, and with two reagent lots. The results are as follows:

	LOB	LOD	LOQ	Acceptable Total Error of LOQ	Claimed measuring range
No. Samples tested	1	4	4		
No.	60	15	15		

Replicates					
ALB	0.002 g/dL	0.003 g/dL	0.50 g/dL	$\leq$ 0.05 g/dL	1.6 – 6.0 g/dL
Ca	0.34 mg/dL	0.36 mg/dL	5.00 mg/dL	$\leq$ 0.32 mg/dL	5.0 – 15.0 mg/dL

e. Analytical specificity:

Serum-Interference studies were performed according to the CLSI EP7-A2 for albumin and calcium analytes. Different concentrations of potential interference substances were spiked into pooled patient serum samples. The sponsor's definitions of no significant interference is <10% difference between the tested and the control samples. Two albumin test concentrations: 3.50 g/dL and 5.00 g/dL, and two calcium test concentrations: 8.00 mg/dL and 12.00 mg/dL were used in these studies. There was no significant interference for albumin and calcium when these analytes and interferents were tested in the concentration ranges indicated in the table below:

Albumin
Triglycerides (up to 3000 mg/dL)
Unconjugated bilirubin (up to 30.0 mg/dL)
Conjugated bilirubin (up to 29.5 mg/dL)
Hemoglobin (up to 500 mg/dL)
Acetaminophen (up to 30 mg/dL)
Ascorbic acid (up to 20mg/dL)
Acetylsalicylic acid (up to 200 mg/dL)
γ globulin (up to 1500 mg/dL)

Calcium
Triglycerides (up to 1119 mg/dL)
Unconjugated bilirubin (up to 30.0 mg/dL)
Conjugated bilirubin (up to 29.5 mg/dL)
Hemoglobin (up to 500 mg/dL)
Magnesium (up to 10.91 mg/dL)
Acetaminophen (up to 30 mg/dL)
Ascorbic acid (up to 20mg/dL)
Acetylsalicylic acid (up to 200 mg/dL)

Triglyceride concentrations greater than 1119 mg/dL were found to interfere with calcium measurement. Therefore the sponsor states in their labeling that a positive bias is observed with triglyceride concentrations above 1119 mg/dL.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Serum and Plasma- Two sets of method comparison studies, serum and plasma, were performed according to the CLSI EP9-A2 guideline. The serum study was completed with 100 albumin (10 spiked and 90 unaltered samples) and 102 calcium human serum samples (9 spiked and 93 unaltered samples) spanning the linear range of the assay. The plasma study was completed with (40) lithium heparinized human plasma samples spanning the linear range of each assay. Each serum and plasma sample was analyzed in singlet using the Selectra ProM analyzer (test method) and in duplicate on the predicates (k921625 - Stanbio Calcium LiquiColor reagent on the SIRRUS analyzer and k063744 - Roche Diagnostics Albumin Gen.2 on the cobas c11 analyzer). Comparison of individual test values versus mean predicate values yielded the following results:

Matrix-Analyte	Slope	Intercept	R^2	Conc. Range Tested
Serum-ALB	0.961	0.122	0.994	1.6 – 5.54 g/dL
Plasma- ALB	0.952	0.251	0.997	1.71 – 5.26 g/dL
Serum- Ca	1.008	-0.001	0.991	5.03 – 14.40 mg/dL
Plasma- Ca	0.992	0.246	0.972	5.47 – 14.76 mg/dL

b. Matrix comparison:

Matrix comparison studies were not performed. See serum and plasma method comparison data above (Section M.2.a.).

The sponsor claimed that lithium heparin plasma is an acceptable anticoagulant.

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:

Reference ranges are provided in the labeling from literature as follows:

	Serum/Plasma
Albumin	3.5 – 5.2 g/dL (Adults) 3.2 – 4.6 g/dL (60-90 years) 2.9 – 4.5 g/dL (90+ years)
Calcium	8.6 – 10.3 mg/dL

Wu, A.H.B., Tietz Clinical Guide to Laboratory Test, 4th Ed., (W.B. Saunders Company), (2006), 66.

Endres, D.B., Rude, R.K., Disorders of Bone, Tietz Fundamentals of Clinical Chemistry, 6th Ed., Burtis, C.A., Ashwood, E.R., Bruns, D.E. (Saunders), (2008), 711.

N. Proposed Labeling:

The labeling is sufficient and does satisfy 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.