

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

A. 510(k) Number:

k132399

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Enzymatic, colorimetric, quantitative

E. Applicant:

ELITechGroup, Inc.

F. Proprietary and Established Names:

ELITech Clinical Systems CREATININE PAP SL
ELITech Clinical Systems ELICAL 2
ELITech Clinical Systems ELITROL I and ELITROL II
ELITech Clinical Systems URINE CONTROL BI-LEVEL

G. Regulatory Information:

Regulation	Classification	Product Code	Panel
21 CFR 862.1225 Creatinine Test system	Class II	JFY	Chemistry (75)
21 CFR 862.1150 Calibrator	Class II	JIX	Chemistry (75)
21 CFR 862.1660 Quality Control material (assayed and unassayed)	Class I, reserved	JJY	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

ELITech Clinical Systems CREATININE PAP SL is intended for the quantitative in vitro diagnostic determination of creatinine in human serum, plasma and urine on ELITech Clinical Systems Selectra Pro Series Analyzers. It is not intended for use in Point of Care settings.

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

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 Pro Series Analyzers.

ELITech Clinical Systems ELITROL I & ELITROL 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 Pro Series Analyzers.

ELITech Clinical Systems URINE CONTROL BI- LEVEL is a set of 2 levels of urine controls used for in vitro diagnostic in the quality control of quantitative ELITech Clinical Systems methods on ELITech Clinical Systems Selectra Pro Series Analyzers.

3. Special conditions for use statement(s):

In vitro diagnostic use only

The test system is not for use in Point of Care settings

4. Special instrument requirements:

ELITech Clinical Systems Selectra ProM Analyzer

I. Device Description:

ELITech Clinical Systems CREATININE PAP SL is available as kit only. It consists of a bi-reagent reagent 1 (R1) and reagent 2 (R2). R1 consists of; MOPS buffer (pH 7.50), EHSPT (N-Ethyl-N-(2-Hydroxy-3-Sulfopropyl)-m-Toluidine), creatinase, sarcosine oxidase, and ascorbate oxidase. R2 consists of: MOPS buffer (pH 7.50), 4-Aminoantipyrine, creatininase, peroxidase, and sodium azide.

ELITech Clinical Systems ELICAL2 is a lyophilized calibrator based on human serum containing constituents to ensure optimal calibration. ELICAL 2 is prepared 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.

ELITech Clinical Systems ELITROL I and ELITROL II are two levels of quality control products consisting of a lyophilized human serum containing constituents at desired levels. ELITROL I and ELITROL II are prepared 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.

ELITech Clinical Systems URINE CONTROL BI-LEVEL is a liquid solution prepared from human urine supplemented with constituents of human and animal origin, chemicals, preservatives and stabilizers. Human sera corresponding to the URINE CONTROL BI-LEVEL were tested for each urine donor and found to be negative for HbsAg and antibodies to HCV and HIV-1/HIV-2 according to FDA-approved methods.

J. Substantial Equivalence Information:

1. Predicate device name(s):

- k024098 – Roche Diagnostics Creatinine plus ver. 2
- k033501 – Roche Calibrator for Automated Systems (C.f.a.s.)
- k041227 – Roche Precinorm and Precipath
- k020817 – Biorad Liquichek Urine Chemistry Control Level 1 and Level 2

3. Comparison with predicate:

Similarities and Differences		
Items	Candidate Device	Predicate Device k024098
	ELITECH Clincial Systems CREATININE PAP SL	Roche Diagnostics Creatinine plus ver. 2
Intended use/Indication for use	Same	For the quantitative determination of the creatinine concentration in serum, plasma, and urine
Test method	Same	Enzymatic colorimetric
Sample type	Serum, plasma (lithium heparin), and urine	Serum, plasma (lithium heparin, Potassium EDTA), and urine
Measuring range	Serum/plasma: 0.10 – 30 mg/dL Urine: 5 – 450 mg/dL	Serum/plasma: 0.06 – 30.5 mg/dL Urine: 1.1 – 452 mg/dL

Similarities and Differences		
Items	Candidate Device	Predicate Device k033501
		ELITECH Clinical Systems ELICAL 2
Intended use/Indication for use	Same	For use in the calibration of quantitative methods on clinical chemistry analyzers
Matrix	Same	Lyophilized serum
Level(s)	Same	Single level
Number of analytes	21	30
Stability	Same	Lyophilized: To store at 2-8°C and protected from light until the expiry date After reconstitution, the stabilities are : - 8 hours between 15-25 °C. - 2 days between 2-8 °C. - 4 weeks between -25 and -15 °C (when frozen once)

Similarities and Differences		
Items	Candidate Device	Predicate Device k041227
		ELITECH Clinical Systems ELITROL I and ELITROL II
Intended use/Indication for use	Same	For use in quality control by monitoring accuracy and precision for quantitative methods
Matrix	Same	Lyophilized serum
Levels	Same	2
Stability	Same	Lyophilized: To store at 2-8°C and protected from light until the expiry date After reconstitution, the stabilities are : - 12 hours between 15-25 °C. - 5 days between 2-8 °C. - 4 weeks between -25 and -15 °C (when frozen once)

Similarities and Differences		
Items	Candidate Device	Predicate Device k020817
	ELITECH Clinical Systems URINE CONTROL BI - LEVEL	Biorad Liquichek Urine Chemistry Control Level 1 and Level 2
Intended use/Indication for use	Same	For quality control in quantitative methods on clinical chemistry analyzers
Matrix	Same	Urine
Levels	Same	2

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

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition. CLSI document EP05-A2, Vol 24, No. 25, August 2004.

Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline. CLSI document EP17-A, vol 24, No. 34, October 2004.

Method Comparison and Bias estimation Using Patient Samples; Approved Guideline—Second Edition. CLSI document EP09-A2-IR, Vol 30, No. 17, July 2010.

Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use: Guidance for Industry and FDA Staff, November 2004.

Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition. CLSI document EP07-A2, Vol 25, No. 27, November 2005.

Evaluation of the Linearity of the Measurement of Quantitative Procedures: a Statistical Approach; Approved Guideline. CLSI document EP06-A, Vol 23, No. 16, April 2003.

L. Test Principle:

Creatininase hydrolyzes creatinine in sample to creatine. Creatine is hydrolyzed by creatinase to sarcosine and urea. Sarcosine is then oxidized by sarcosine oxidase to produce hydrogen peroxide (H₂O₂). H₂O₂ reacts with 4-amino-antipyrine (4-AAP) and EHSPT (N-Ethyl-N-2(-Hydroxy-3-Sulfopropyl)-m- Toluidine) under the catalytic action of peroxidase to form a colored quinoneimine. The absorbance of the quinoneimine at 546 nm is proportional to the concentration of creatinine in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A precision study was performed by assaying three serum pools at 3 concentrations over 20 operating days, on two Selectra PROM analyzers and with two lots of reagent. Assay runs were performed twice per day and each sample was tested in duplicate. Calibration was performed for each run. The results are summarized below:

Serum

Samples	n	Mean (mg/dL)	Within-run		Total	
			SD	CV(%)	SD	CV(%)
pool 1	80	0.76	0.01	1.2	0.01	1.9
pool 2	80	1.52	0.01	0.6	0.03	1.7
pool 3	80	5.52	0.03	0.5	0.08	1.5

Urine

Samples	n	Mean (mg/dL)	Within-run		Total	
			SD	CV(%)	SD	CV(%)
pool 1	80	83	1	0.8	2	2.2
pool 2	80	159	1	0.7	4	2.3
pool 3	80	308	6	1.9	9	2.9

b. Linearity/assay reportable range:

A linearity study across the claimed assay range was performed by preparing samples from patient serum pools at a low creatinine concentration and a high concentration. The low pool contained serum diluted with albumin/NaCl (6 g/dL/0.9%). Eleven samples in all were assayed in triplicate

The expected values were plotted against the observed values and a linear regression line was fitted with the following regression equation:

Serum

Level	Expected value	Mean value
1	0.18	0.10
2	3.20	3.23
3	6.22	6.21
4	9.24	9.20
5	12.26	12.22
6	15.28	15.31
7	18.30	18.43

8	21.32	21.46
9	24.34	24.41
10	27.36	27.27
11	30.38	30.25

$$y = 0.9893x + 0.08, r = 1.0000$$

Based on these results, the sponsor claims that the assay is linear from 0.10 – 30 mg/dL.

Urine

Level	Expected value	Mean value
1	5	5
2	50	50
3	95	96
4	140	138
5	185	185
6	230	228
7	276	281
8	321	322
9	366	364
10	411	407
11	456	457

$$y = 1.0195x - 3, r = 0.9999$$

Based on these results, the sponsor claims that the assay is linear from 5 – 450 mg/dL.

The sponsor has also provided data to support that post auto dilution the extended range claim is 30 - 150.00 mg/dL for serum

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

Stability

Real-time testing was conducted. The stability study protocol and the acceptance criteria have been reviewed and found to be acceptable. The study results support the following stability claims in the labeling:

Item	Storage Conditions		Claimed Stability
Reagent Packs	Closed-vial	2 – 8 °C	20 months
	Open-vial	On board	28 days
Calibrator	Closed-vial	2 – 8 °C	11 months
	Open-vial	15 – 25 °C	8 hours
		2 – 8 °C	2 days

		-25 to -15 °C (frozen once)	4 weeks
Serum Controls	Closed-vial	2 – 8 °C	30 months
	Open-vial	15 – 25 °C	12 hours
		2 – 8 °C	5 days
		-25 to -15 °C (frozen once)	4 weeks
Urine Controls	Closed-vial	2 – 8 °C	24 months
	Open-vial	2 – 8 °C	30 days

The creatinine in ELICAL 2 is traceable to ID-MS (Isotope dilution-Mass Spectrometry) and was previously cleared under k103376

The serum control materials ELITROL I and ELITROL II were previously cleared under k103376

URINE CONTROL BI –LEVEL

Value Assignment

The target value is determined by the median of 80 results from 2 Selectra ProM analyzers. The median is acceptable to the sponsor when percentage deviation is less than 10%.

Calibration frequency

Stability across a 14-day calibration interval was assessed by calculating the percentage bias of 2 urine control specimens on each day from the result obtained on day 0. The results support the calibration interval claims of 14 days. The sponsor also noted in the labeling that a recalibration is recommended when reagent lots change, and when quality control results fall outside the range established, and after a maintenance operation.

d. Detection limit:

Limit of Blank (LoB) and Limit of Detection (LoD) were determined following CLSI guideline EP17-A. For LoB determination, albumin/NaCl (6 g/dL/0.9%) was used as the zero sample and assayed 60 times on 2 selectra ProM analyzers. For LoD determination, 4 diluted serum or urine samples with creatinine concentrations between LoB and 4 * LoB were assayed 15 times for each sample (N = 60).

For LoQ determination, 4 low concentration samples were prepared by saline dilution and were assayed 15 times each (N = 60). The CV% and the SD at each tested concentration were calculated. The sponsor's acceptable total error for the determination Limit of Quantification is ≤ 0.02 and 4 mg/dL for serum and urine, respectively. If the confidence interval is within the acceptable total error limits, then the Limit of Quantification is acceptable.

Summary:

Based on the limit of quantitation determined in this study (see result in the below table) and the result from the linearity study in M1.b., the sponsor's labeling claims a measuring range of 0.1 to 30 mg/dL for serum and 5 to 450 mg/dL for urine..

	LoB	LoD	LoQ
Serum	0.01	0.02	0.08
Urine	0.2	0.5	2.0

e. Analytical specificity:

Testing for interfering substances was based on CLSI EP-7A. Testing was performed on a minimum of six concentrations for each interfering substance. Two different clinically relevant concentrations of creatinine (1.50 and 5.00 mg/dL) were used for evaluation. Samples with increasing amounts of potential interferents were tested in triplicate and compared to a control sample without the interferent.

The sponsor defined non-significant interference as the highest level tested that does not cause $\geq \pm 10\%$ change between the tested samples and the control sample.

Serum

Analyte	Highest concentration tested with no significant interference (mg/dL) ($\leq 10\%$)
Triglyceride	3000
Unconjugated Bilirubin	30.0
Conjugated Bilirubin	14.8
Hemoglobin	500
Glucose	500
Creatinine	5.0
Uric acid	20
Ascorbic Acid	20.0

Calcium dobesilate, Methyl-dopa and L-dopa cause falsely low results at therapeutic concentrations.

Urine

Analyte	Highest concentration tested with no significant interference (mg/dL) ($\leq 10\%$)
Conjugated Bilirubin	29.5
Hemoglobin	500
Ascorbic Acid	20.0
Methyl dopa	10
Calcium dobesilate	50.0

Glucose	5000
pH	2.5 – 12

A summary of these results and interferences is found in the labeling.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Serum

The performance of the Creatinine PAP SL reagent on the Selectra ProM analyzer was compared with the Roche Creatinine plus v2 reagent on the cobas c111 analyzer. Study performed according to CLSI protocol EP9-A2 using 100 serum samples covering the measuring range with values from 0.10 to 30.1 mg/dL. The linear regression results are summarized below:

	Regression parameters	Confidence Interval, 95%	
		Lower 95%	Upper 95%
slope	0.979	0.977	0.981
Intercept	0.05	0.03	0.07
r	1.000		

Urine

The performance of the Creatinine PAP SL reagent on the Selectra ProM analyzer was compared with the Roche Creatinine plus v2 reagent on the cobas c111 analyzer. Study performed according to CLSI protocol EP9-A2 using 54 urine samples covering the measuring range with values from 5 – 413 mg/dL. The linear regression results are summarized below:

	Regression parameters	Confidence Interval, 95%	
		Lower 95%	Upper 95%
slope	1.063	1.055	1.070
Intercept	2	1	3
r	1.000		

b. Matrix comparison:

To demonstrate comparable performance between serum, and lithium heparin, 40 matched samples were compared with the Creatinine PAP SL reagent on the Selectra ProM analyzer. Study performed according to CLSI protocol EP9-A2 covering the measuring

range with values from 0.11 to 29.49 mg/dL. The linear regression results are summarized below:

	Regression parameters	Confidence Interval, 95%	
		Lower 95%	Upper 95%
slope	0.994	0.990	0.997
Intercept	0.00	-0.03	0.03
r	1.000		

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):*

None

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Matrix	Men	Women
Serum, mg/dL	0.72 - 1.18	0.55 - 1.02
Serum, $\mu\text{mol /L}$	64 - 104	49 - 90
Urine, mg/kg/24h	14 - 26	11 - 20
Urine, $\mu\text{mol/kg/24h}$	124 - 230	97 - 177

Newman, D.J., Price C.P., Tietz Fundamentals of Clinical Chemistry, 5th Ed., Burtis, C.A. & Ashwood, E.R. (W.B. Saunders eds. Philadelphia USA), (2001), 414.

Ceriotti, F., Reference Intervals for Serum Creatinine Concentrations: Assessment of Available Data for Global Application. Clin. Chem., (2008), 54, 559.

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.