

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

A. 510(k) Number:

k113269

B. Purpose for Submission:

New Device

C. Measurand:

Alkaline phosphatase

D. Type of Test:

Quantitative, enzymatic colorimetric

E. Applicant:

ELITechGroup

F. Proprietary and Established Names:

ELITech Clinical Systems ALP IFCC SL

G. Regulatory Information:

1. Regulation section:
21 CFR § 862.1050; alkaline phosphatase/isoenzymes test system
2. Classification:
Class II
3. Product code:
CJE; Nitrophenylphosphate, alkaline phosphatase or isoenzymes test system
4. Panel:
Clinical Chemistry (75)

H. Intended Use:

1. Intended use:
See Indications for Use
2. Indications for use:
ELITech Clinical Systems ALP IFCC SL is intended for the quantitative *in vitro* diagnostic determination of alkaline phosphatase in human serum and plasma on ELITech Clinical Systems Selectra analyzers.

It is not intended for use in Point of Care settings.

Alkaline phosphatase or its isoenzymes measurements are used in the diagnosis and treatment of liver, bone, parathyroid and intestinal diseases.

3. Special conditions for use statements:
 - For prescription use only
 - For *in vitro* diagnostic use only
 - For use in clinical laboratories only
4. Special instrument requirements:
ELITech Clinical Systems Selectra ProM Analyzer

I. Device Description:

ALP IFCC SL is available as a kit only. It consists of 2 reagents, R1 and R2. Reagent 1 contains 2-Amino-2-methyl-1-propanol (AMP) buffer (pH 10.45), Magnesium ions (2.4 mM), and Zinc ions (1.2 mM). Reagent 2 contains *p*-Nitrophenylphosphate (*p*-NPP; 80 mM) and sodium azide (<0.1%).

J. Substantial Equivalence Information:

1. Predicate device name(s):
Roche Diagnostics ALP2S (Alkaline phosphatase acc. to IFCC Gen. 2)
2. Predicate k number(s):
k033185

3. Comparison with predicate:

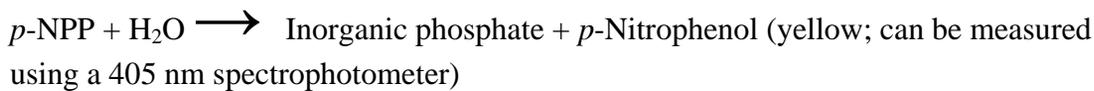
	<u>ELITech Clinical Systems Device</u> (ALP IFCC SL) (k113269)	<u>Predicate device</u> (Roche Diagnostics ALP2S) (k033185)
Intended use	Same	<i>In vitro</i> test for the quantitative determination of alkaline phosphatase in human serum and plasma.
Indication for Use	Same	Alkaline phosphatase or its isoenzymes measurements are used in the diagnosis and treatment of liver, bone, parathyroid and intestinal diseases.
Appearance of reagents	Same	Liquid form, ready to use
Sample type	Same	Serum Lithium heparinized plasma
Assay Principle	Same	Colorimetric
Reagent storage	Same	Store at 2-8 °C the reagent is stable until the expiry date stated on reagent.
Instrument	Selectra ProM Analyzer	Cobas c111
Measuring range	20 – 1023 U/L	3 – 1200 U/L
Calibration Frequency	1 day	5 days
On board stability	1 day	10 days
Calibrator	Recommended calibration material (not included): ELITech Clinical Systems ELICAL 2	Recommended calibration material (not included): Roche Calibrator f.a.s.
Controls	Recommended quality control material (not included): ELITech Clinical Systems ELITROL I (Normal control) ELITech Clinical Systems ELITROL II (Pathologic control)	Recommended quality control material (not included): Roche Precinorm U Roche Precipath U

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

- CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition
- CLSI EP06-A: Evaluation of the Linearity of the Measurement of Quantitative Procedures: a Statistical Approach
- CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition
- CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline
- CLSI EP09-A2: Method Comparison and Bias estimation Using Patient Samples; Approved Guideline—Second Edition

L. Test Principle:

In the presence of Mg^{2+} , Zn^{2+} and AMP as a phosphate acceptor, alkaline phosphatase hydrolyzes *p*-nitrophenyl phosphate substrate into inorganic phosphate and *p*-nitrophenol (yellow compound with an absorbance peak at 405 nm). The rate of the formation of *p*-nitrophenol is directly proportional to the alkaline phosphatase activity as follows:



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

This study followed the CLSI EP5-A2 “Evaluation of Precision Performance of Clinical Chemistry Devices” guideline. Within-run and Total Precision studies were performed for alkaline phosphatase. Studies were performed by conducting 2 runs per day, two measurements per run, for 3 levels of serum-based samples and 2 levels of controls, on 2 Selectra ProM analyzers for 20 operating days. Data for level 1 is from a diluted human serum pool sample, level 2 is from a natural serum pool sample, and level 3 is from a spiked human serum pool sample. Two lots of reagent were used for the study. The results are summarized in the table below:

ALP Levels	Level 1	Level 2	Level 3	Elitrol I	Elitrol II
No. of Samples	80	80	80	80	80
No. of Replicates (per run)	2	2	2	2	2
Mean (U/L)	57	144	262	82	224
Total SD	2.5	5.4	7.7	2.2	6.4
Total %CV	4.4	3.8	2.9	2.6	2.8
Within-Run SD	0.8	1.3	1.5	0.6	1.9
Within-Run %CV	1.3	0.9	0.6	0.7	0.8

b. Linearity/assay reportable range:

A linearity study was conducted based on the CLSI EP06-A guideline by comparing observed versus expected values for 11 equally-spaced serum samples. Two pools of patient serum samples were prepared to obtain one high and one low concentration. A high concentration of sample was obtained by spiking the serum pool (1023 U/L) and a low concentration of sample was prepared by diluting the sample pool with buffered saline solution (20 U/L). Using the high and low pooled samples, eleven levels of inter-mixtures with equidistant activities were prepared, with all samples assayed in triplicate on one Selectra ProM instrument. Data was analyzed using 1st, 2nd, and 3rd order least square regressions. A 1st order linear regression was generated as follows:

T	Slope	Intercept	R ²	r	Standard Error (U/L)	Concentration Ranges tested
eALP	0.9681	3.1406	0.9996	0.9998	7	20-1023 U/L

The results of the study support the sponsor's claim that the ALP IFCC SL assay is linear across the measuring range of 20 to 1023 U/L.

Dilution Study:

The sponsor performed a 1:10 manual dilution study with 10 spiked samples using saline as the diluent. Ten spiked serum samples with ALP analyte concentrations between 991 and 9874 U/L were diluted 1:10. The % recoveries between the expected and observed values are within 10%. Therefore, the sponsor claimed that the ALP concentration greater than the upper claimed measuring range (1023 U/L) can be diluted manually 1:10 with saline.

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

Traceability: The sponsor claims that the Elitech ALP IFCC SL assay is traceable to the IFCC formulation (Tietz, 1983), by manual measurement.

Stability of the reagent: The shelf-life of ALP IFCC SL reagents is 18 months (tested using 2 lots) when stored at 2 to 8°C. The shelf-life stability is based on their real-time stability study, which is still on-going. The on-board stability and calibration frequency is 1 day. Shelf-life and on-board stability study protocols have been provided and found to be adequate.

d. *Detection limit:*

The Limits of Blank (LoB), Detection (LoD) and Quantitation (LoQ) studies were conducted following the CLSI EP17-A guideline for ALP IFCC SL. Two Selectra Pro M analyzers and two lots of a validated reagent were used. The LoB values were determined by analyzing a blank sample 60 times using 2 reagent lots over 2 analyzers over multiple days. The LoD and LoQ studies each used 4 diluted sample pools prepared from 4 different patient sample pools of known activities in order to obtain an activity close to four times the calculated value of the LoB or the expected LoQ, respectively. LoD and LoQ values were determined by measuring each of the 4 diluted sample pools 15 times (measuring low activity of analyte for LoD and samples diluted in saline for LoQ) in one run across two analyzers using two reagent lots on multiple days (2-5 days). Results are summarized below:

	LoB	LoD	LoQ
Detection Limits	4 U/L	6 U/L	20 U/L

e. *Analytical specificity:*

Interference studies were performed according to the CLSI EP7-A2 guideline for alkaline phosphatase. Seven to nine increasing concentrations of potential interferents, tested in triplicate, were spiked into low (150 U/L), medium (250 U/L), and high (900 U/L) levels of pooled patient serum samples. The sponsor's definition of no significant interference is $\leq 10\%$ difference between the tested and the control samples. There was no significant interference between alkaline phosphatase and interferents in the concentration ranges indicated in the table below:

Interferents	Highest level tested with no interference
Triglycerides	3141 mg/dL
Unconjugated bilirubin	30.0 mg/dL, (513 μ mol/L)
Conjugated bilirubin	29.5 mg/dL, (504 μ mol/L)
Hemoglobin	500 mg/dL
Ascorbic acid	20.0 mg/dL
Acetylsalicylic acid	200 mg/dL
Acetaminophen	30 mg/dL

The sponsor notes in the label that other compounds may interfere based on 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:*

A method comparison study was performed using the ALP IFCC SL reagent on a Selectra ProM analyzer and Roche Diagnostics Alkaline phosphatase acc. to IFCC Gen.2 reagent on a cobas c111 analyzer according to the CLSI EP09-A2 guideline. A total of 100 serum patient samples were used, including 5 diluted and 5 spiked samples. The sample range tested on the candidate device was 20 to 1023 U/L. The result of the linear regression is shown below:

Slope (95% Confidence Interval)	Intercept (95% Confidence Interval)	r	R ²
1.025 (1.017 to 1.034)	0.909 (-4 to 3)	0.998	0.997

b. *Matrix comparison:*

A matrix comparison study was performed with 40 paired serum and plasma (in lithium heparin) samples using one Selectra ProM analyzer, according to the CLSI EP09-A2 guideline. Two samples were diluted and 3 samples were spiked. The sample range tested was 21 to 878 U/L. The result of the linear regression is shown below:

Slope (95% Confidence Interval)	Intercept (95% Confidence Interval)	r	R ²
1.10 (1.096 to 1.111)	-3 (-5 to -1)	1.000	0.999

Based on the data, the sponsor claims that lithium heparin is an acceptable anticoagulant for the collection of plasma samples.

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:

Expected values are cited from “Panteghini, M., Bais, R., *Enzyme*, Tietz Fundamentals of Clinical Chemistry, 6th Ed., Burtis, C.A., Ashwood, E.R., Bruns, D.E., (Saunders), (2008), 317.”

	Men:	Women:
20-50 years old:	53-128 U/L	42-98 U/L
≥ 60 years old:	56-119 U/L	53-141 U/L

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.