

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

A. 510(k) Number:

k100547

B. Purpose for Submission:

New device

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, immuno-turbidimetric method enhanced by latex particles

E. Applicant:

Seppim S.A.S.

F. Proprietary and Established Names:

ELITech Clinical Systems HbA1c

ELITech Clinical Systems HbA1c Calibrator Set

ELITech Clinical Systems HbA1c Control L+H

G. Regulatory Information:

1. Regulation section:

21CFR 864.7470

21CFR 862.1150

21CFR 862.1660

2. Classification:

Class II, II, and I reserved

3. Product code:

LCP, JIT, JJX

4. Panel:

Hematology (81), Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

ELITech Clinical Systems HbA1c is intended for use in the quantitative *in vitro* diagnostic determination of hemoglobin A1c (HbA1c) in human whole blood on Vital Scientific Selectra/Flexor Analyzers. It is not intended for use in Point of Care settings.

HbA1c measurements are used for the monitoring of long term blood glucose control in diabetic patients.

ELITech Clinical Systems HbA1c Calibrator Set is a calibrator with 4 different levels of values for in vitro diagnostic use in the calibration of quantitative ELITech Clinical Systems HbA1c on Vital Scientific Selectra/Flexor Analyzers as specified in the instructions for use.

ELITech Clinical Systems HbA1c Control L+H is a quality control with 2 levels of values (Low and High values) for in vitro diagnostic use in accuracy control of quantitative ELITech Clinical Systems HbA1c on Vital Scientific Selectra/Flexor Analyzers as specified in the instructions for use.

3. Special conditions for use statement(s):

- For prescription use only
- Should not be used for the diagnosis of diabetes mellitus
- Should not be used in judging the day-to-day glucose control
- Should not be used to replace daily home testing of blood glucose
- Should not be used during pregnancy, in hemolytic diseases, or following recent significant blood loss

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.

I. Device Description:

The ELITech Clinical Systems HbA1c reagent is available only as a kit that consists of 3 reagents: Reagent R1 is ready to use and contains suspended latex particles (0.13%) in a buffer with stabilizers and sodium azide (<0.1%); Reagent R2a and Reagent R2b are mixed to prepare a working reagent, Reagent 2. This mixture contains mouse anti-human HbA1c monoclonal antibody and goat anti-mouse IgG polyclonal antibody in a buffer containing stabilizers and sodium azide (<0.1%); Reagent R3 is a ready to use hemolysis reagent in an aqueous solution containing a stabilizer and sodium azide (<0.1%).

The ELITech Clinical Systems HbA1c Calibrators Set consists of 4 levels of calibrators (Cal 1, Cal 2, Cal 3, Cal 4) containing approximately 5.0%, 7.9%, 10.9%, and 13.7% HbA1c. Each level consists of lyophilized hemolysates prepared from human erythrocytes to yield 0.5 mL each after reconstitution.

The ELITech Clinical Systems HbA1c Control L+H is a 2 level quality control product consisting of lyophilized hemolysates prepared from human erythrocytes containing HbA1c levels of 4.1-6.1% and 10.2-13.2 %.

The calibrators and controls are listed in the reagent labeling as required but not provided.

The following is included in the labeling for both the calibrators and controls: All human material should be considered as potentially infectious. All products derived from blood are prepared exclusively from the blood of donors tested individually by FDA-approved methods and found to be negative for HbsAg and antibodies to HCV and HIV1/HIV2. However, as no test method can rule out the potential risk of infection with absolute certainty, handle cautiously as potentially infectious.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Pointe Scientific, Inc. Hemoglobin A1c Reagent Set;

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

k031539

3. Comparison with predicate:

Similarities and Differences		
Item	ELITech Clinical Systems (HbA1c) (candidate device)	Pointe Scientific Hemoglobin A1c Reagent Set (predicate device k031539)
Intended Use	For <i>in vitro</i> diagnostic use in the quantitative determination of hemoglobin A1c (HbA1c) in human whole blood	Same
Specimen Type	Whole Blood (EDTA)	Whole Blood (Venous blood with EDTA)
Standardization	Values are defined in reference to NGSP values and are traceable to IFCC reference method	Traceable to NGSP and IFCC
Assay Principle	Immuno-turbidimetry enhanced by latex particles using a two-reagent reaction sequence	Same
Measuring Range	2.5 to 16%	2.0 to 16%
Instrument	The Vital Scientific Selectra Junior Analyzer (also trademarked as the Vital Scientific Flexor Junior Analyzer)	Pointe Scientific Hitachi Instruments (model 717 or 917)

Similarities and Differences		
Item	ELITech Clinical Systems HbA1c Calibrators Set (candidate device)	Pointe Scientific Hemoglobin A1c Calibrator Set (predicate device k031539)
Intended Use	For <i>in vitro</i> diagnostic use in the calibration of quantitative ELITech Clinical Systems HbA1c	Same
Calibrator Levels	4 levels	Same
Matrix / Ingredients	Lyophilized hemolysates from human erythrocytes	Same
Preparation	Reconstitute with DI water before use	Same
Storage	2 – 8°C	Same
Reconstituted Vial / Use	30 days stored at 2 – 8°C	Same

Stability		
Item	ELITech Clinical Systems HbA1c Control L+H (candidate device)	Pointe Scientific Hemoglobin A1c Control Set (predicate device k031539)
Intended Use	For <i>in vitro</i> diagnostic use in accuracy control of quantitative ELITech Clinical Systems HbA1c	Same
Control Levels	2 levels	Same
Matrix / Ingredients	Lyophilized hemolysates from human erythrocytes	Hemolysate prepared from packed human erythrocytes
Preparation	Reconstitute with DI water before use	Same
Storage	2 – 8°C	Same
Reconstituted Vial / Use Stability	30 days stored at 2 – 8°C	Same

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

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (CLSI EP9-A2)

Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A)

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition (CLSI EP5-A2)

Determination of Limits of Detection and Limits of Quantification; Approved Guideline (CLSI EP17-A)

L. Test Principle:

The ELITech Clinical Systems HbA1c assay is an immuno-turbidimetry methodology enhanced by latex particles using a two-reagent reaction sequence.

1st reaction: The sample is mixed with reagent R1. Total hemoglobin and HbA1c have the same absorption affinity for these particles, the %HbA1c present in the sample is proportional to latex-bound HbA1c.

2nd reaction: Addition of the working Reagent R2 leads to agglutination complexes, formed from the interaction between latex-bound HbA1c and the corresponding

antibodies. Turbidity created by these aggregates is proportional to the amount of latex-bound HbA1c and therefore is proportional to the %HbA1c in the samples. A non-linear calibration curve is used to obtain the %HbA1c.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The sponsor performed precision studies in accordance with the CLSI EP5-A2 (Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition) guideline. Three levels of human patient sample pools (whole blood collected on EDTA) at a low, medium and high level of HbA1c were analyzed in duplicate with 2 runs per day over 20 days on the Vital Scientific Selectra Junior analyzer. The results are presented in the table below:

Sample	N	Mean (% A1c)	Within Run		Total Imprecision	
			SD	%CV	SD	%CV
Low Level	80	4.4	0.05	1.1	0.10	2.3
Medium Level	80	6.7	0.06	0.9	0.13	1.9
High Level	80	9.5	0.10	1.0	0.28	2.9

b. *Linearity/assay reportable range:*

Linearity across the assay range was assessed by testing two levels of marketed whole blood based control samples at low (2.3%) and high (16%) HbA1c concentrations. Ten test samples with equidistant concentrations were prepared by mixing the two level samples. Each sample was tested in triplicate on the Vital Scientific Selectra Junior analyzer. Data was analyzed using 1st, 2nd and 3rd order least square regression analysis in accordance with the CLSI EP6-A (Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach; Approved Guideline) guideline. The difference in predicted values between the first and second order models are as follows:

$$1^{\text{st}} \text{ order: } y = 1.53x + 1.10$$

$$2^{\text{nd}} \text{ order: } y = -0.04x^2 + 1.94x + 0.29$$

The sponsor chose the 2nd order regression because it is significant and the results are shown in the table below:

Levels	Mean	Predicted 1st order	Predicted 2nd order	Difference 2nd-1st	% Difference
1	2.3	2.6	2.2	-0.4	<u>a</u>
2	4.0	4.2	4.0	-0.1	-2.5%
3	5.7	5.7	5.8	0.1	1.7%
4	7.5	7.2	7.5	0.2	2.7%
5	9.0	8.8	9.1	0.3	3.3%
6	10.7	10.3	10.6	0.3	2.8%
7	12.0	11.8	12.1	0.2	1.7%
8	13.5	13.4	13.4	0.1	0.7%
9	14.8	14.9	14.8	-.01	-0.7%
10	15.9	16.4	16.0	-0.4	-2.5%

a: Percentage not calculated since the acceptance for very low concentration is given in units (+/- 0.4% HbA1c standardized against NGSP/DCCT reference method).

Based on the data, the sponsor claimed that the assay's linearity range is 2.5 to 16.0% HbA1c.

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

Traceability:

The sponsor supplied a "Certificate of Traceability" from the National Glycohemoglobin Standardization Program (NGSP) demonstrating that the ELITech Clinical Systems HbA1c assay on the Vital Scientific Selectra Junior with ELITech Clinical Systems HbA1c Calibrators (Cal 1, Cal 2, Cal 3, Cal 4) has met NGSP requirements. The NGSP certification requires annual renewal. The current list of NGSP certified methods is available on the following website: <http://www.ngsp.org/prog/index.html>

Value Assignment

ELITech SEPPIM receives the previously cleared (k031539) Calibrator set with 4 levels (Cal 1, Cal 2, Cal 3, Cal 4) and two levels of Control material (Control L+H) from a commercial vendor as closed, unlabeled vials and labels the vials without further modifying or opening them. The calibrator and control material are traceable to NGSP verified material.

ELITech Clinical Systems HbA1c Calibrator concentrations included in the labeling are those provided by commercial vendor. The concentrations are verified by measurement in replicates of 4 using the ELITech Clinical

Systems HbA1c assay and the Vital Scientific Selectra/Flexor Junior Analyzer. The mean values are used to assess the adequacy of recovery. The observed mean must be within the target range provided on the commercial product.

ELITech Clinical Systems HbA1c Control L+H target ranges included in the labeling are those provided by commercial vendor. SEPPIM verifies the target ranges through their own Quality control procedure by testing in triplicate using the ELITech Clinical Systems HbA1c assay and the Vital Scientific Selectra/Flexor Junior. The mean values are used to assess the adequacy of recovery. The observed mean must be within the target range provided on the commercial product.

Stability

Calibrator material (Cal 1, Cal 2, Cal 3, Cal 4) is purchased from a commercial vendor (previously cleared under k033501). The sponsor claims that when stored at 2-8°C and protected from light, the calibrators, prior to reconstitution, are stable until the expiration date printed on the label. After reconstitution, the calibrators are stable for 30 days when stored at 2-8°C. The labeling states that the open vials should be stored tightly capped and should not be frozen.

Control material (Control L+H) is purchased from a commercial vendor (previously cleared under k041227). The sponsor claims that when stored at 2-8°C and protected from light, the calibrators, prior to reconstitution, are stable until the expiration date printed on the label. After reconstitution, the calibrators are stable for 30 days when stored at 2-8°C. The labeling states that the open vials should be stored tightly capped and should not be frozen.

On-board stability for the ELITech Clinical Systems HbA1c assay was established by real time studies on the Vital Scientific Selectra/Flexor Junior and demonstrated on-board reagent stability of 14 days. The ELITech Clinical Systems HbA1c is stable until the expiration date printed on the label when stored at 2 to 8°C.

d. Detection limit:

The sponsor performed a limit of detection (LoD) study according to the CLSI EP-17-A guideline. The limit of the blank (LoB) was determined by analyzing a blank sample 60 times on a Vital Scientific Selectra Junior Analyzer. The results demonstrated that the LoB is 0.6%. The LoD was determined by analyzing 4 low level HbA1c diluted samples (2.4%) 15 times each on a Vital Scientific Selectra/Flexor Junior analyzer. The LoD of 0.7% was determined using the median minus the 5th percentile plus the LoB value.

The claimed measuring range, 2.5% to 16% HbA1c, is based on the linearity study summarized in M.1.b above.

e. *Analytical specificity:*

Studies were performed to assess common or known substances that could interfere with the ELITech Clinical Systems HbA1c Reagent on the Vital Scientific Selectra Junior analyzer. Two patient blood sample pools with 7.0% and 10% HbA1c were spiked with multiple concentrations of potential interfering substances. Samples containing various concentrations of potential interferents were tested and the results compared to those obtained from control samples containing no potential interferent. The percent difference between the control sample and the sample spiked with the potential interferent was no greater than $\pm 10\%$ for concentrations at or below those listed in the following table:

Potential interfering substance	Concentration at which no significant interference ($\leq 10\%$) was observed
Bilirubin (conjugated)	≤ 29.5 mg/dL
Bilirubin (unconjugated)	≤ 30 mg/dL
Triglyceride	≤ 2035 mg/dL
Acetylsalicylic acid (Aspirin)	≤ 200 mg/dL
Ascorbic acid (Vitamin C)	≤ 20.0 mg/dL
Rheumatoid Factor	≤ 1008 IU/mL

Hemoglobin Variants HbS, HbC, HbD, HbE, HbF and HbA2:

Potential cross-reactivity to hemoglobin variants was examined using patient samples containing known concentrations of HbA1c and the variants (HbS, HbC, HbD, HbE, HbF and HbA2). Each sample was tested in duplicate, and the difference between the known concentration (from the European Primary Reference laboratory, a member of the NGSP network) and the values obtained with the candidate assay on the Vital Scientific Selectra/Flexor Junior were calculated.

No significant bias of greater than $\pm 10\%$ was observed in the presence of HbS, HbC, HbD, HbE or HbA2.

Samples with HbF concentrations $> 9\%$ demonstrated significant bias ($> \pm 10\%$). The labeling states that high concentrations of HbF up to 9% showed no significant interference. The presence of 20% HbF produced a negative bias of -21.5%.

Carbamylated, Acetylated and Labile HbA1c:

Pooled patient blood samples with HbA1c concentrations of 6% and 9.0% were spiked with sodium cyanate (used to carbamylate), aspirin (used to acetylate) and glucose (labile HbA1c). Samples were measured in triplicate

using the candidate assay on the Vital Scientific Selectra/Flexor Junior and the differences between the spiked sample and the unspiked control sample were calculated.

No significant interference ($\geq \pm 10\%$) was observed with sodium cyanate up to 10 mmol/L, aspirin up to 10 mmol/L, or glucose up to 1000 mg/dL.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed using 40 whole blood patient samples collected in EDTA with HbA1c concentrations ranging from 4.6% to 14.0% using the comparative method. Each sample was tested in duplicate with the Pointe Scientific HbA1c on the Cobas Mira (predicate) and using the ELITECH HbA1c reagent on the Vital Scientific Selectra/Flexor Junior. The candidate device results (Y) were compared to the corresponding predicate results (X) and regression analysis resulted in: $y = 0.926x + 0.056$; $R^2 = 0.968$.

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):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The sponsors have included the following in the labeling with the corresponding literature references:

	NGSP/DCCT (%)	IFCC (mmol/mol)
Non-diabetics	4.0-6.0	20-42

- American Diabetes Association , Standards of Medical Diabetes Care in Diabetes-2008, *Diabetes Care* (2008); 31 Suppl 1, S12.
- Weykamp, C et al., *Clinical chemistry*, (2008), 54, 240.

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.