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

A. 510(k) Number:

k182702

B. Purpose for Submission:

New Device

C. Measurand:

Creatine Kinase

D. Type of Test:

Quantitative, enzyme assay

E. Applicant:

SEKISUI DIAGNOSTICS P.E.I. INC.

F. Proprietary and Established Names:

SEKURE Creatine Kinase Assay

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1215 - Creatine phosphokinase/creatine kinase or isoenzymes test system
2. Classification:
   Class II
3. Product code:
   CGS
4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   For the in vitro quantitative measurement of creatine kinase activity in serum and plasma on the SK500 Clinical Chemistry System. Measurements of creatine kinase are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

3. Special conditions for use statement(s):

   For in vitro diagnostic and prescription use only.

4. Special instrument requirements:

   SK500 Clinical Chemistry Analyzer

I. Device Description:

The SEKURE Creatine Kinase Assay (CK Assay) is a spectrophotometric, coupled enzyme assay for the quantitative measurement of creatine kinase (CK) activity. The assay consists of two working reagents.

Creatine Kinase Buffer Reagent (R1)	A solution containing a buffer (pH 6.0), 60 mmol/L Imidazole, 27 mmol/L glucose, 27 mmol/L NAC, 14 mmol/L magnesium acetate, 2 mmol/L EDTA·Na_2, 2.7 mmol/L NADP, ≥5 kU/L hexokinase (yeast)
Creatine Kinase Substrate Reagent (R2)	A solution containing 160 mmol/L Imidazole, 11mmol/L ADP, 28 mmol/L AMP, 55 μmol/L Ap5A, ≥14 kU/L G-6-PDH (microbial), 2 mmol/L EDTA·Na_2, 160 mmol/L creatine phosphate.

Testing is performed on the SK500 Clinical Chemistry Analyzer with calibrator and controls which are provided separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Creatine Kinase-SL Assay

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

   k973999

3. Comparison with predicate:

Item	SEKURE Creatine Kinase Assay (Candidate Device)	Creatine Kinase-SL Assay (k973999) (Predicate Device)
Intended Use	For the in vitro quantitative measurement of creatine kinase activity	Same
Assay principle	Colorimetric (NADPH), Enzymatic (coupled hexokinase-G6PD)	Same
Sample Type	Serum and lithium heparinized plasma	Serum
Analytical Range	11 to 1500 U/L	2 to 1500 U/L
Analyzers	SK500 Clinical Chemistry Analyzer	Hitachi 717 Analyzer

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

CLSI EP05-A3, Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline, 3rd Edition.

CLSI EP06-A, Evaluation of Linearity of Quantitative Measurement Procedures: a Statistical approach, 1st Edition.

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, 2nd Edition.

CLSI EP07-A2, Approved Guideline Interference Testing in Clinical Chemistry, 2nd Edition.

L. Test Principle:

The SEKURE CK Assay employs the reverse reaction of CK, to produce adenosine triphosphate (ATP). The reaction is coupled to hexokinase and G6PDH which consumes ATP to generate NADPH. The rate of NADPH formation is monitored at 340 nm and is directly proportional to CK activity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Testing was conducted following the recommendations in the CLSI EP05-A3 guideline using two lots of SEKURE CK reagents on one SK500 analyzer. Two levels of sera controls, one level of pooled serum, and three levels of pooled plasma were assayed in duplicate in two runs a day for twenty (20) days. The precision study results are summarized below.

Lot	Sample	N	Mean CK (U/L)	Repeatability		Total	
				SD	%CV	SD	%CV
Lot 1	Serum Control 1	80	145.3	1.6	1.1	2.5	1.7
	Serum Control 2	80	438.1	3.2	0.7	6.0	1.4
	Serum High Pool	80	772.2	5.3	0.7	13.4	1.7
	Plasma Low Pool	80	155.9	1.9	1.2	3.4	2.2
	Plasma Med Pool	80	372.3	3.1	0.8	7.7	2.1
	Plasma High Pool	80	576.5	3.4	0.6	20.0	3.5
Lot 2	Serum Control 1	80	143.3	1.7	1.2	2.4	1.7
	Serum Control 2	80	436.9	3.3	0.8	5.3	1.2
	Serum High Pool	80	773.9	4.8	0.6	13.8	1.8
	Plasma Low Pool	80	153.5	2.0	1.3	3.3	2.1
	Plasma Med Pool	80	370.6	2.6	0.7	7.2	1.9
	Plasma High Pool	80	574.2	3.8	0.7	20.4	3.6

b. Linearity/assay reportable range:

Linearity studies were performed following the recommendations in the CLSI EP06-A guideline. Linearity testing for serum was conducted using eight dilutions of pooled high serum sample with saline to generate a CK activity range from 0 - 1650 U/L. Linearity testing for plasma was conducted using ten dilutions and admixtures of pooled plasma to generate a CK activity range from 3 - 2700 U/L. Testing of all samples was conducted in quadruplicate using two lots of SEKURE CK reagent on one SK500 analyzer. Deviation of the mean observed value from the calculated theoretical value was determined for each sample in the series. The maximum deviation from linearity observed was <11%. The linearity study data supports the claimed measuring range for the SEKURE CK Assay of 11 to 1500 U/L for serum and plasma.

Dilution Recovery Studies:

The sponsor provided data supporting their claim that creatine kinase sample values above the assay measuring range can be accurately determined by diluting (3x) in

saline and assaying with the SEKURE Creatine Kinase-SL Assay.

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

The SEKURE Creatine Kinase Assay is traceable to an IFCC reference method.

d. *Detection limit:*

Limits of detection studies were performed following the recommendations in the CLSI EP17-A2 guideline.

The Limit of Blank (LoB) was determined as the 95th percentile of measurements of blank samples. The Limit of Detection (LoD) was determined as the lowest amount of analyte in a sample detected with a 95% probability. Testing was conducted by analyzing low level samples (saline blanks and dilutions of pooled serum or plasma in saline) in quadruplicate for three days (12 replicates per sample) producing 60 measurements total. All samples were assayed on two lots of SEKURE CK reagents and one SK500 analyzer. The LoB and LoD were determined individually for each reagent lot, dilution level, and matrix type.

The Limit of Quantitation (LoQ) testing was conducted using eight linear serum samples and eight linear plasma samples, ranging from normal (~100 U/L) to zero on two SEKURE CK reagent lots. Each sample was assayed in quadruplicate on five runs over three days to give 40 replicates per sample. The LoQ was determined as the lowest CK activity value at which the %CV was ≤20%.

The results of the evaluation of the detection limits and final claim are summarized in the following table:

Analyte	LoB	LoD	LoQ
CK (U/L)	3	5	11

e. *Analytical specificity:*

An interference study was performed following the recommendations in the CLSI EP07-A2 guideline to assess common or known substances that could interfere with the CK Assay. Interference testing was conducted using two lots of SEKURE CK reagent on one SK500 analyzer. All interferents were evaluated at CK concentrations of 180 and 415 U/L using serum samples. A minimum of seven concentrations of interferent were assessed. Each sample was tested in replicates of five on each reagent lot and compared to a control sample. Significant interference was defined by the sponsor as a percent difference greater than 10% from control.

Results are summarized in the table below:

Interferent	Highest Concentration at which no significant interference was observed
Hemoglobin	200 mg/dL
Conjugated Bilirubin	40mg/dL

Interferent	Highest Concentration at which no significant interference was observed
Unconjugated Bilirubin	40 mg/dL
Intralipid	1000 mg/dL
Ascorbic acid	3.0 mg/dL

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 114 serum specimens were tested in duplicate over eight operating days on the candidate and predicate device. Two samples were excluded from the data analysis as they exceeded the reportable range of the assay. The remaining 112 serum specimens had a CK range of 28 to 1409 U/L. Five of the samples included in the data analysis were spiked to evaluate the high end of the assay measuring interval. First replicate data collected on the candidate method and mean sample data collected on the predicate method were evaluated using Deming regression analysis and gave the following equation:

$y = 0.964\ x + 2.4$ U/L, $r = 0.9998$

b. Matrix comparison:

Matrix comparison testing was conducted to evaluate the suitability of lithium heparin plasma with the SEKURE CK Assay on the SK500 analyzer. A set of 75 matched serum and lithium heparin plasma specimens were assayed in duplicate using two lots of CK reagents on one SK500 analyzer. Thirteen of these samples were contrived samples. The CK activity ranged from 38 to 1487 U/L. Deming regression analysis was generated using first replicate data from plasma and mean sample values from serum and gave the following equation:

$y = 1.015\ x$ -3.4 U/L, $r = 0.9991$

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:

A reference range verification study for the SEKURE CK Assay was performed using serum and lithium heparin plasma on the SK500 Clinical Chemistry Analyzer. The data provided supports the literature reference range[(1)].

Males: 46-171 U/L (37°C)
Females: 34-145 U/L (37°C)

[(1)] Rifai, N.; Horvath, A.R.; Wittwer, C., (Eds). Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Sixth Edition. Elsevier, St. Louis, Missouri (2018), p. 409-11.

The labeling states that these values are suggested guidelines and it is recommended that each laboratory establish the normal range for the area in which it is located.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.