K141265

510(k) Summary

JUL 18 2014

ENVOY®500 CK REAGENT KIT

1.	Date:	May 12, 2014
2.	Submitter:	ELITech Clinical Systems SAS Zone Industrielle 61500 SEES FRANCE
3.	Contact Person:	Debra K. Hutson Manager, RA/QA, ELITechGroup, Inc. 21720 23rd Dr SE, Suite 150 Bothell, WA 98021 Phone: 425-482-5174 Fax: 425-482-5550 Email: d.hutson@elitechgroup.com
4.	Device Description: Classification	ENVOY®500 CK REAGENT KIT Class II JHW Clinical Chemistry 21 CFR 862.1215
5.	Predicate Device:	K122083 ELITech Clinical Systems SAS ELITech Clinical Systems CK NAC SL

6. Intended Use

Reagents: Envoy 500 CK Reagent is for the quantitative *in vitro* diagnostic determination of creatine kinase (CK) in human serum and plasma using the Envoy 500 Chemistry System. It is not intended for use in Point of Care settings.

Measurements of creatine phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

Special conditions for use statement(s):
Prescription Use Only. It is not intended for use in Point of Care settings.

Special instrument requirements:
Performance is provided for the ENVOY® 500 Analyzer.

7. **Device Descriptions**
ENVOY CK REAGENT KIT is available as kit only. It consists of a bi-reagent R1 and R2 whose composition,

for R1: 125 mmol/L Imidazole buffer, pH 6.10; 25 mmol/L D-Glucose; 25 mmol/L N-Acetyl-L-Cysteine; 12.5 mmol/L Magnesium acetate; 2.4 mmol/L NADP; 2.0 mmol/L EDTA; ≥ 6800 U/L Hexokinase (microorganism); < 0.1% Sodium azide

for R2: 250 mmol/L Creatine phosphate; 15.2 mmol/L ADP; 25 mmol/L AMP; 103 µmol/L Diadenosine pentaphosphate; ≥ 8800 U/L G-6-PDH (microorganism); < 0.1% Sodium azide.

8. **Substantial Equivalence Information - Assay (reagent)**
1. Predicate Device Name
   ELITech Clinical Systems CK NAC SL
2. K122083
3. Comparison with predicate

Similarities

Parameter	ELITech Clinical Systems Device ENVOY® 500 CK REAGENT KIT	Predicate Device ELITech Clinical Systems CK NAC SL K122083
Intended Use / Indication for Use	Intended for the quantitative in vitro diagnostic determination of creatine kinase (CK) in human serum and plasma using the Envoy 500 Chemistry System. It is not intended for use in Point of Care settings. Measurements of creatine	Intended for the quantitative in vitro diagnostic determination of creatine kinase (CK) in human serum and plasma on ELITech Clinical Systems Selectra analyzers. It is not intended for use in Point of Care settings. Measurements of creatine

Parameter	ELITech Clinical Systems Device ENVOY® 500 CK REAGENT KIT	Predicate Device ELITech Clinical Systems CK NAC SL K122083
	phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.	phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.
Composition	**Reagent R1:** 125 mmol/L Imidazole buffer, pH 6.10; 25 mmol/L D-Glucose; 25 mmol/L N-Acetyl-L-Cysteine; 12.5 mmol/L Magnesium acetate; 2.4 mmol/L NADP; 2.0 mmol/L EDTA; ≥ 6800 U/L Hexokinase (microorganism); < 0.1% Sodium azide **Reagent R2:** 250 mmol/L Creatine phosphate; 15.2 mmol/L ADP; 25 mmol/L AMP; 103 µmol/L Diadenosine pentaphosphate; ≥ 8800 U/L G-6-PDH (microorganism); < 0.1% Sodium azide.	Same
Appearance of reagents	Liquid form, ready to use	Same
Specimen Type	Serum, plasma	Same
Reagent storage	Store at 2-8 °C and protect from light. The reagent is stable until the expiry date stated on the label.	Same
Expected values	Serum/plasma: Men: < 171 U/L Women: < 145 U/L	Same
Assay Technology	UV Method Kinetic based on IFCC recommendations	Same
Assay Range	10 to 1714 U/L	Same
Interferences	**Triglycerides:** No significant interference up to 3000 mg/dL. **Unconjugated bilirubin:** No significant interference up to 30.0 mg/dL (513 µmol/L). **Conjugated bilirubin:** No significant interference up to 29.5 mg/dL (504 µmol/L).	Same

Parameter	ELITech Clinical Systems Device ENVOY® 500 CK REAGENT KIT	Predicate Device ELITech Clinical Systems CK NAC SL K122083
	Ascorbic acid: No significant interference up to 20.0 mg/dL. **Acetaminophen:** No significant interference up to 30.0 mg/dL. **Acetylsalicylic acid:** No significant interference up to 200.0 mg/dL. **Hemolysis:** No significant interference up to 100 mg/dL of hemoglobin	
On Board stability	28 days	Same
Limit of quantification (LoQ)	5 U/L	5 U/L

Differences

Parameter	ELITech Clinical Systems Device ENVOY®500 CK REAGENT KIT	Predicate Device ELITech Clinical Systems CK NAC SL
Instrument	ENVOY®500 Analyzer	Selectra ProM Analyzer
Calibrator	None. The Envoy 500 uses a calibration factor for this assay.	Recommended calibration material (not included): ELITech Clinical Systems ELICAL 2
Limit of detection (LoD)	2 U/L	1 U/L
Precision	**Within run** Level 138 U/L CV= 1.5% Level 375 U/L CV= 1.0% Level 1135 U/L CV= 1.4% **Total** Level 138 U/L CV= 3.6% Level 375 U/L CV= 3.5% Level 1135 U/L CV= 3.6%	**Within run** Level 147 U/L CV= 0.7% Level 406 U/L CV= 1.1% Level 1154 U/L CV= 1.1% **Total** Level 147 U/L CV= 1.7% Level 406 U/L CV= 2.4% Level 1154 U/L CV= 3.9%
Method comparison	y= 1.050 x + 0 U/L r= 0.998 range: 14 to 1650 U/L	y= 1.012 x + 2 U/L r= 0.998 range: 11 to 1712 U/L
Control	Recommended: Envoy Serum Control kit (k111063)	Recommended: ELITROL I (normal control) and ELITROL II (abnormal control)

9. **Standard/Guidance Document Reference**

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition. CLSI (NCCLS) document EP05-A2, Vol 24, No. 25, August 2004.
- 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 (NCCLS) 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 (NCCLS) document EP06-A, Vol 23, No. 16, April 2003.
- NF EN 13640:2002 Stability Testing of in vitro Diagnostic Reagents

10. **Test Principle:**

Kinetic determination of creatine Kinase (CK) activity:
(Kinetic_UV method, based on IFCC recommendations).

$$\text{Creatine Phosphate} + \text{ADP} \xrightarrow{\text{Creatine kinase}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{D-Glucose} \xrightarrow{\text{Hexokinase}} \text{D-Glucose-6-Phosphate} + \text{ADP}$$

$$\text{G-6-P} + \text{NADP}^{+} \xrightarrow{\text{G-6-PDH}} \text{D-Gluconate-6-Phosphate} + \text{NADPH} + \text{H}^{+}$$

G-6-P: D-Glucose-6-Phosphate
G-6-PDH: Glucose-6-Phosphate Dehydrogenase.

The rate of increase in absorbance of NADPH is measured at 340 nm and is directly proportional to the activity of CK in the sample.

11. **Performance Characteristics – Analytical Performance**

a. Precision/Reproducibility

The precision of the device was determined in accordance with Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition. CLSI (NCCLS) document EP05-A2, Vol 24, No. 25, August 2004.

Within-run and total precision results were obtained by performing two runs per day, two measures per run, for 3 levels of samples on 2 instruments during twenty operating days according to CLSI EP05-A2 protocol. The results are presented in the table below:

Precision

Serum

Level	n	Mean (U/L)	Precision %	
			Within-run CV%	Total CV%
Level 1	80	138	1.5	3.6
Level 2	80	375	1.0	3.5
Level 3	80	1135	1.4	3.6

b. Linearity/assay reportable range

The linearity study of ENVOY®500 CK Reagent Kit Reagent was performed according to CLSI protocol EP06-A.

Serum

Eleven (11) levels of patient pools were prepared from a high activity sample obtained by spiking a serum pool and a low activity sample obtained by dilution to obtain 11 levels with equidistant activities. The samples were measured and experimental values are compared to expected values.

This study demonstrates acceptable linearity from 10-1714 (with an acceptable deviation from linearity of ±10%).

Automatic dilution 1 to 10 allows an upper linearity of ENVOY500 CK reagent to 17140 U/L.

c. Traceability

ENVOY®500 CK Reagent Kit is calibrated automatically by the Envoy 500 through the use of a calibration factor in the instrument parameters. The calibration factor has traceability to the IFCC method. Results are automatically calculated by the factor. The original CK reagent cleared for use on Envoy 500 also makes use of a calibration factor (k112416).

Envoy Serum Control kit was cleared under k111063 (which included creatine kinase as an analyte).

d. Stability

Real-time stability:
The shelf-life of ENVOY®500 CK Reagent Kit has been followed real time for 14 months on 3 different lots.

On board stability: This evaluates the period of time during which correct measurements are obtained after installation of a new vial on board.

At least 3 levels of sample (high/medium/low) are tested in duplicate at Day 0.

Four (4) activities levels are analyzed in duplicate, until the deviations from the results at D0 are higher than acceptance criteria or for at least 30 days. During this period, the reagents are stored on the analyzer (vial open).

This study was performed on one (1) lot on ENVOY500 analyzer. The results indicate that the reagent is stable 28 days on board.

e. Detection limit

Determined according to CLSI protocol EP17-A (Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline).

Limit of Detection:
The limit of Detection was obtained from 15 measurements of 4 samples prepared from 4 patient samples measured using ENVOY®500 CK reagent and diluted with Albumin 6 g/dL / NaCl 0.9% to obtain an activity of approximately 3.5 U/L.
The data are not Gaussian, so LoD= LoB + DS,β (where DS,β is determined by calculating the median minus the 5th percentile of the low activity sample distribution).

Limits of Quantification:
The limit of Quantification was obtained from 15 measurements of 4 samples prepared from 4 patient samples measured using ENVOY®500 CK reagent and diluted with Albumin 6 g/dL / NaCl 0.9% to obtain an activity of 5 U/L.
Acceptance criteria: The acceptable performance goal is defined as the lowest measured value with a precision coefficient of variation of ≤ 15%.

Serum

Limit of Detection (LoD) of ENVOY®500 CK Reagent Kit obtained from 15 measurements of 4 samples with a low activity of analyte (approximately 4 x LoB ≈ 3.5 U/L) is 2 U/L.

Limit of Quantification (LoQ) of ENVOY®500 CK Reagent Kit obtained from 15 measurements of 4 samples at nominal activity is 5 U/L.

f. Interference/analytical specificity

Interferences due to hemolysis, unconjugated bilirubin, conjugated bilirubin, triglycerides, ascorbic acid, acetylsalicylic acid, acetaminophen were investigated following the recommended sample levels in CLSI EP07-A2 protocol (Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition).

For each potential interferent tested, 2 serum sample pools at two creatine kinase levels close to those specified in Appendix B of EP7-A2 were prepared:
-1st pool: low activity at nominal 150 U/L
-2nd pool: high activity at nominal 1200 U/L
Aliquots of each of the serum sample pools were spiked with increasing interferent concentration. Test ranges covered at least the interferent level specified in Appendix D of EP7-A2. Thus, there were two series of interferent spike for each potential interferent tested. A control sample was prepared from the sample pool diluted in the appropriate diluent.

Interferent	Test range	# of different concentrations tested
Triglycerides	up to 3000 mg/dL	9
Unconjugated bilirubin	up to 30.0 mg/dL	7
Conjugated bilirubin	up to 29.5mg/dL	7
Ascorbic acid	up to 20 mg/dL	7
Acetylsalicylic acid	up to 200 mg/dL	7
Acetaminophen	up to 30 mg/dL	7
Hemoglobin	Up to 556 mg/dL	8

Two (2) levels of control (Serum control Level 1 and Serum control Level 2) were tested to check the reagents.
For both sample pools for each interferent, each point was measured in triplicate per run.
Acceptance criteria: an accepted bias of ±10% in sample pools with low (150U/L) or high (1200U/L) nominal activity.

The results of testing interferences are the following:

- Concentration up to 100 mg/dL of hemoglobin, 30.0 mg/dL unconjugated bilirubin, 3000 mg/dL triglycerides, 20 mg/dL ascorbic acid, 29.5 mg/dL conjugated bilirubin, 200 mg/dL acetylsalicylic acid 30 and mg/dL acetaminophen do not show any significant interference for each substance.
- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.

The following statement will also be included in the labeling:

Other compounds may interfere. Users should refer to the two 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.

12. **Performance Characteristics – Comparison Studies**

a. Method comparison

A correlation study was performed between ENVOY®500 CK Reagent kit on ENVOY®500 analyzer and ELITech Clinical Systems CK NAC SL on Selectra ProM analyzer according to CLSI EP09-A2 protocol (Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second edition).

This study was performed using 100 serum patient samples from 14 to 1650 U/L over a span of 5 days.

Regression analysis of the results yielded the following:

y = 1.050x + 0 U/L
r = 0.998
r^2 = 0.996
Standard error of the estimate Sy.x = 28 U/L

b. Comparison study

To support the use of lithium heparin plasma samples, a second correlation study was performed between ENVOY®500 CK Reagent kit on ENVOY®500 analyzer and ELITech Clinical Systems CK NAC SL on Selectra ProM analyzer according to CLSI EP09-A2 protocol (Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second edition).

This study was performed using 40 plasma specimens (in lithium heparin), ranging from 10 to 1660 U/L over a span of 2 days.

Regression analysis of the results yielded the following:

y = 1.020x + 3 U/L
r = 0.999
r^2 = 0.999
Standard error of the estimate Sy.x = 21 U/L

c. Expected values/Reference Range

As indicated in the instructions for use for ENVOY®500 CK Reagent Kit, each laboratory should establish and maintain its own reference values. The values given are used as guidelines only.

	Men	Women	
Serum/ Plasma	< 171	<145	U/L

These reference values are from:
Schumann, G., *et al.*, Clin. Chem. Lab. Med., (2002), 40, 635-42

d. Clinical Studies:

Not applicable

e. Clinical Cut-off:

Not applicable

13. **Conclusion**

The information on the principle and performance of the device that is contained in this premarket notification is complete and supports a decision that our device is substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

ELITECHGROUP
DEBRA HUTSON
MANAGER, RA/QA
21720 23RD DR SE, SUITE 150
BOTHELL WA 98021

July 18, 2014

Re: K141265
Trade/Device Name: ENVOY 500 CK Reagent Kit
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine phosphokinase/creatine kinase or isoenzymes test system
Regulatory Class: II
Product Code: JHW
Dated: May 14, 2014
Received: May 15, 2014

Dear Ms. Debra Hutson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

k141265

Device Name
ENVOY®500 CK REAGENT KIT

Indications for Use *(Describe)*

ENVOY®500 CK REAGENT KIT is intended for the quantitative in vitro determination of creatine kinase (CK) in human serum and plasma using the ENVOY 500 Chemistry System.

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

Creatine phosphokinase and its isoenzymes measurements are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Ruth A. Chesler -S

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