

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

A. 510(k) Number:

K050644

B. Purpose for Submission:

Clearance to market an ELISA assay for human cardiac Troponin I

C. Measurand:

Troponin I

D. Type of Test:

Quantitative measurement of Troponin I via ELISA assay

E. Applicant:

Vancouver Biotech Ltd.

F. Proprietary and Established Names:

VBL Serum Troponin I ELISA Test

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:

MMI

4. Panel:

H. Intended Use:

1. Intended use(s):

The VBL Serum Troponin I ELISA Test is intended for the quantitative determination of cardiac Troponin I in human serum. Measurement of Troponin I values are useful in the evaluation of acute myocardial infarction (AMI).

2. Indication(s) for use:

The VBL Serum Troponin I ELISA Test is intended for the quantitative determination of cardiac Troponin I in human serum. Measurement of Troponin I values are useful in the evaluation of acute myocardial infarction (AMI).

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

None

I. Device Description:

The VBL Serum Troponin I ELISA Test is a quantitative enzyme immunoassay that provides an assay for the quantitative measurement of Troponin I. The test kit can be used together with other diagnostic methods to assess cardiac damage caused by AMI.

The VBL Serum Troponin I ELISA Test is based on the principle of a solid phase enzyme-linked immunosorbent assay. The assay utilizes micro titer wells coated with three monoclonal anti-TnI antibodies. The fourth monoclonal antibody is in the antibody-horseradish peroxidase (HRP) conjugate solution. The test sample is allowed to react simultaneously with the four antibodies, and the troponin I molecules are sandwiched between the immobilized and enzyme-linked antibodies. Addition of a chromogen, which reacts with the horseradish peroxidase, results in a color proportional to the concentration of Troponin I.

J. Substantial Equivalence Information:

1. Predicate device name(s):

AxSYM Troponin I test

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

K974103

3. Comparison with predicate:

Similarities		
Item	Device – K050644	Predicate- K974103
Analyte	Troponin I	Troponin I
Antibody	Murine	Murine
Intended Use	The evaluation of acute myocardial infarction	The evaluation of acute myocardial infarction

Differences		
Item	Device	Predicate
Assay Design	ELISA - a microtiter well enzyme immunoassay	MEIA - microparticle enzyme immunoassay
Number of binding antibodies	3 on the solid phase (well)	1 on the microparticle
Peroxidase bound conjugate antibody	Murine	Goat

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

CLSI EP15-A: User Demonstration of Performance for Precision and Accuracy; Approved Guideline

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

The VBL Serum Troponin I ELISA Test is a solid-phase, enzyme-linked immunoassay. The assay utilizes four unique monoclonal antibodies directed against distinct antigenic determinants on the troponin-I molecule. The three mouse anti-troponin-I antibodies are used for solid phase immobilization, while the fourth antibody is in the horseradish peroxidase conjugate solution. The patient sample is allowed to react simultaneously with the four antibodies, resulting in the formation of a “sandwich” between the solid-phase and the enzyme linked antibodies. The solid phase is washed to remove unbound label and a substrate/chromogen solution is added. The TnI concentration is proportionate to the intensity of the color development which is measured spectrophotometrically.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Using procedures outlined in CLSI EP15-A, the intra-assay precision was evaluated in patient serum samples that contained 2, 5, 10, 20, 50, and 100 ng/mL Troponin I by running 20 replicates of each sample in one run. Percent CVs ranged from approximately 4.87% near the cutoff to approximately 2.52% at 100 ng/ml Troponin I. In the same samples, the inter-assay precision, (24 replicates of each sample over 24 runs) ranged from approximately 7.20% to less than 1% CV.

b. *Linearity/assay reportable range:*

Linearity of the assay was established by comparison to the predicate device and further evaluated experimentally following EP06-A: Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline. The company measured 10 different known Troponin I concentrations spanning the range of their assay. They measured each point in triplicate. Increasing the order of their calibration fit did not change the agreement with the predicate or evaluation of a clinical outcome. The reported range for the assay was determined primarily by the limitations of the readout device, a spectrophotometer. Saturation of the spectrophotometer determined the upper concentration limit while statistical noise in the blank determined the lower limit of the assay.

For Troponin I by VBL Serum Troponin I ELISA assay, the method has been demonstrated to be linear from 0.5 ng/ml to 100 ng/ml.

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

Calibrators packaged with the assay are traceable to standards of calibrated with purified Human Cardiac Troponin I.

d. *Detection limit:*

Following the methods outlined in CLSI EP17-A, the sponsor determined that “zero plus 2 sigma” lower limit of detection for their assay was 0.27 ng/ml. The sponsor is claiming a lower limit of detection of 0.5 ng/mL.

e. *Analytical specificity:*

The company demonstrated that their assay did cross-react with human cardiac troponin T, human skeletal muscle troponin T, and human skeletal muscle troponin I. The assay was free from interference at the following levels:

Analyte	Test Concentration
Rabbit skeletal muscle troponin C	2,500 ng/ml
Human cardiac troponin T	2,500 ng/ml
Human skeletal muscle troponin T	2,500 ng/ml
Human skeletal muscle troponin I	2,500 ng/ml
Hemoglobin	200 mg/ml
Biotin	200 ng/ml
Bilirubin	1 mg/ml

In addition, the assay was tested and shown to be free from interference at the 10 µg/ml level from the following materials:

Analyte (10 µg/ml Final Concentration)	
Acetaminophen	Digitonin
Acetylsalicylic acid	Digoxin
Adenine	Dopamine
Albumin (bovine)	Erythromycin
Alloprinolol	Gentistic Acid
Ambroxol	Isoproterenol
Ampicillin	Isosobide dinitrate
Ascorbic Acid	Nifedipine
Atenolol	Nystatin
Atropine	Oxazepam
Caffeine	Oxytetracycline
Captopril	Propanolol
Chloramphenicol	Theophiline
Cinnarizine	L-Thyroxine
Cyclophosphamide	Urea
Cyclosporine	Uric Acid
	Verapamil

In addition, the assay was free from interference effects at the following levels:

Analyte	Concentration
Heparin	14 IU/mL
Warfarin	10 µg/mL
EDTA	18 mg/mL
Red Blood Cells	< 100 per mL
Hemolysate	< 0.05%
Total proteins	30mg/mL

f. Assay cut-off:

The clinical cut-off of 1.5ng/mL of Troponin I was determined based on published literature and the clinical specificity and sensitivity analyses of a clinical study (see below).

2. Comparison studies:

a. *Method comparison with predicate device:*

The sponsor conducted a statistical study comparing the submitted device to the predicate using serum samples taken from patients admitted for emergency care. The company used a total of 212 patient samples in their study. In a concentration range spanning 0ng/ml to 71 ng/ml Troponin I, the proposed assay yielded a linear correlation with the predicate of 0.9512, a slope of 1, and an intercept of 0.034 ng/ml.

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

In a clinical study of 212 patients, 110 of whom were clinically diagnosed as having experienced an acute myocardial infarction, the assay demonstrated a clinical sensitivity of 98% as compared to a WHO diagnosis.

b. *Clinical specificity:*

In a clinical study of 212 patients, 110 of whom were clinically diagnosed as having experienced an acute myocardial infarction, the assay demonstrated a clinical specificity of 98% as compared to a WHO diagnosis.

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:

Serum levels of cardiac Troponin I are extremely low in normal, healthy individuals. The sponsor states that more than 98% of the normal population had Troponin I levels below the cutoff 91.5 ng/mL) of their assay. Serum concentrations of 1.5 ng/ml Troponin I or higher, as measured by the VBL Serum Troponin I ELISA Test, are indicative of an acute myocardial infarction (AMI).

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 substantial equivalence decision.