

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

A. 510(k) Number:

k051925

B. Purpose for Submission:

New product

C. Measurand:

Troponin I, CK-MB, Myoglobin

D. Type of Test:

Qualitative lateral flow immunochromatographic test

E. Applicant:

Access Bio Inc.

F. Proprietary and Established Names:

CareStart Cardiac 3-in-1 Troponin I/CK-MB/Myoglobin Test

CareStart Cardiac 2-in-1 Troponin I/Myoglobin Test

CareStart Cardiac Troponin I

CareStart Cardiac CK-MB

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1215, Creatine phosphokinase/creatin kinase or isoenzymes test system

21 CFR §866.5680, Myoglobin immunological test system

2. Classification:

Class II

3. Product code(s):

MMI, JHT, DDR

4. Panel:

Clinical Chemistry (75)

Immunology (82)

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

“**CareStart™ Cardiac Troponin I Test** is intended for the qualitative detection of cardiac troponin I in human blood, serum, or plasma. Measurement of cardiac troponin I aids in rapid diagnosis of acute myocardial infarction. The performance characteristics of the test have not been evaluated in a point-of-care (POC) setting.”

“**CareStart™ Cardiac CKMB Test** is intended for the qualitative detection of cardiac CKMB in human blood, serum, or plasma. Measurement of cardiac CKMB aids in rapid diagnosis of acute myocardial infarction. The performance

characteristics of the test have not been evaluated in a point-of-care (POC) setting.”

“**CareStart™ Cardiac 2-in-1 Troponin I/Myoglobin Test** is intended for the qualitative detection of cardiac troponin I, and myoglobin in human blood, serum, or plasma. Measurement of cardiac troponin I, and myoglobin aids in rapid diagnosis of acute myocardial infarction. The performance characteristics of the test have not been evaluated in a point-of-care (POC) setting.”

“**CareStart™ Cardiac 3-in-1 Troponin I/CKMB/Myoglobin Test** is intended for the qualitative detection of cardiac troponin I, CKMB and myoglobin in human blood, serum, or plasma. Measurement of cardiac troponin I, CKMB and myoglobin aids in rapid diagnosis of acute myocardial infarction. The performance characteristics of the test have not been evaluated in a point-of-care (POC) setting.”

3. Special conditions for use statement(s):
For prescription use only.
4. Special instrument requirements:
None.

I. Device Description:

The device consists of a plastic housing that contains a chromatographic membrane strip, a red blood cell separating membrane, and a dye pad impregnated with monoclonal antibodies. There is a well for application of the sample, and a results window where the test line and control line appear. Each test is packaged in a sealed pouch.

J. Substantial Equivalence Information:

1. Predicate device name(s):
LifeSign MI® CK-MB/Myoglobin/Troponin I Rapid Test
2. Predicate 510(k) number(s):
k981882
3. Comparison with predicate:
Both assays: are lateral flow immunoassays, are qualitative one-step assays, detect the same antigens, have the same result format including an internal control indicator, use the same specimens, have similar monoclonal antibodies, and have the same time-to-read.

The assays differ in the cutoff values; the predicate cutoff values are myoglobin 50 ng/mL, CK-MB 5 ng/mL, troponin I 1.5 ng/mL. The assays differ in sample volume; the predicate requires 120 uL while the proposed assay requires 80 uL whole blood or 60 uL of serum or plasma.

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

None referenced.

L. Test Principle:

The proposed *CareStart*™ Cardiac Tests are solid-phase chromatographic immunoassays for qualitative detection of cardiac troponin I, CKMB, and/or myoglobin. After patient sample is added to the sample well, red blood cells, if present, are removed by a built-in membrane. Analyte(s) in the remaining sample makes a complex with dye-labeled analyte-specific antibody and a separate analyte-specific biotinylated antibody. This complex migrates through the test area containing immobilized streptavidin. The antibody-dye-analyte-biotinylated antibody binds to the streptavidin in the test area. Unbound dye complexes migrate out of the test area and are captured in the control area.

Pinkish-purple band(s) will appear in the test area if the concentrations of the given analyte is (are) above the cutoff value: troponin I 0.6 ng/mL, myoglobin 70 ng/mL, CKMB 5.0 ng/mL. A band must be present in the control area for a valid test.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Three operators each tested 10 replicates of a negative serum sample and a positive serum sample containing troponin I, 0.7 ng/mL, CK-MB, 6 ng/mL, and/or myoglobin, 80 ng/mL. Sixty (60) uL of serum was added to the sample well and the result was read at 15 minutes. All four device configurations were tested and found to have 100% agreement between the expected and observed results, with no discrepancy between the operators.

b. *Linearity/assay reportable range:*

Not applicable. These tests are intended for qualitative use.

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

Current claimed shelf stability is 8 months at room temperature.

d. *Detection limit:*

See Assay Cutoff section below.

e. *Analytical specificity:*

Related human proteins at the concentrations below were added to normal human serum and tested in triplicate with all test configurations; all results were negative.

Related Protein	Test Level
CK-MM	1000
CK-BB	1000
Human cardiac troponin C	1000
Human cardiac troponin T	1000
Human skeletal muscle troponin I	300

Potentially interfering endogenous substances at the concentrations below were added to normal serum samples spiked with troponin I, CK-MB, or myoglobin at the cutoff value and a negative control and tested in triplicate with all test configurations; all results were as expected.

Endogenous Analyte	Test Level
Human albumin	10 g/dL
Bilirubin	40 mg/mL
Hemoglobin	2 g/dL
Ttriglycerides	1000 mg/dL

Potentially interfering exogenous substances at the concentrations below were added to normal serum and serum spiked with troponin I (0.7 ng/mL), CK-MB (6 ng/mL), and/or myoglobin (80 ng/mL) according to the test configuration. All tests with normal serum samples returned negative results. All positive samples with the exception of verapamil in the Cardiac 3-in-1 configuration returned positive results. In this configuration, verapamil suprathreshold levels gave an equivocal result, although verapamil was positive in the other three test configurations.

Interferent	Concentration (ug/mL)		Interferent	Concentration (ug/mL)
Acetaminophen	1000		Indomethacin	100
Acetylsalicylic acid	2000		Isosorbide dinitrate	100
Allopurinol	500		L-thyroxine	100
Ambroxol	500		Methaqualone	100
Ampicillin	6000		D, L-a-Methyl dopa	500
Ascorbic acid	50		Nicotinic acid	3000
Atenolol	50		Nifedipine	1000
Caffeine	50		Nitrofurantoin	200
Captopril	200		Noraminopyrine	500
Chloramphenicol	6000		Nystatin	13,000 *
Chlordiazepoxide	200		Oxazepam	50
Cinnarizine	500		Oxytetracycline	500
Cyclosporine	1000		Phenobarbital	30
Diclofenac	100		Probenecid	1000
Digoxin	800		Procainamide	2000
Dipyridamole	2000		Quinidine	1000
Dopamine	400		Sulfmethoxazol	1000
Erythromycin	2000		Theophylline	500
Furosemide	100		Trimethoprim	200
Glibenclamide	10		Verapamil	200
Hydrochlorothiazide	100			* U/mL

The effect of different sample volumes on the performance of the assay configurations was tested. Plasma aliquots ranging from 40 to 100 uL and whole blood aliquots ranging from 60 to 100 uL were tested in duplicate with positive and negative controls; all tests read correctly in all test configurations.

Hematocrits ranging from 20% to 70% did not interfere with test results when normal (negative) blood and spiked positive blood were tested in duplicate in all assay configurations.

f. *Assay cut-off:*

Normal human blood was supplemented with the three analytes at concentrations around the cutoff. Each configuration of the analytes was tested 20 times, with the same results that are summarized in the table below:

Performance of CareStart around Assay Cutoffs				
	Concentration of Analyte (ng/mL)			
Troponin I (ng/mL)	0	0.3	0.6	1.2
# Positives	0/20	4/16	19/20	20/20
% Positives	0	20%	95%	100%
CK-MB (ng/mL)				
0	2.5	5.0	10.0	
# Positives	0/20	5/15	19/20	20/20
% Positives	0	25%	95%	100%
Myoglobin (ng/mL)				
0	35	70	140	
# Positives	0/20	3/17	20/20	20/20
% Positives	0	15%	100%	100%

2. Comparison studies:

a. *Method comparison with predicate device:*

Performance of the various test configurations was compared to the predicate in samples from 73 individuals admitted to a hospital emergency room with chest pain and an additional 100 samples from healthy subjects. Results from the CareStart 3-in-1 Troponin I/CKMB/Myoglobin Test are shown below; results were the same for the other configurations:

		Agreement between CareStart 3-in-1 Test and Predicate					
		Predicate Device					
		Troponin I		CK-MB		Myoglobin	
		Pos	Neg	Pos	Neg	Pos	Neg
CareStart 3-in-1 Test	Pos	54	2	59	2	53	2
	Neg	0	117	1	111	0	118

	Troponin I	CK-MB	Myoglobin
Positive Agreement	100%	98.3%	100%
Negative Agreement	98.3%	98.2%	98.3%
Overall Agreement	98.8%	98.3%	98.8%

Performance of the various test configurations was compared to the results obtained from the DPC Immulite Myoglobin test and the Dade Behring Dimension CK-MB (MMB) and Troponin I (CTNI) test from the 73 clinical samples. Results from the CareStart 3-in-1 Troponin I/CKMB/Myoglobin Test are shown below; results were the same for the other configurations:

Agreement between CareStart 3-in-1 Test and Quantitative Methods

		Dimension CTNI		Dimension MMB		Immulite Myoglobin*	
		≥ 0.6	< 0.6	≥ 5	< 5	≥ 70	< 70
CareStart 3-in-1 Test	Pos	55	1	54	2	41	1
	Neg	1	16	1	16	1	9

* n =52

	Troponin I	CK-MB	Myoglobin
Positive Agreement	98.2 %	98.2 %	97.6 %
Negative Agreement	94.1 %	88.9 %	90.0 %
Overall Agreement	97.3 %	95.9 %	96.2 %

b. Matrix comparison:

Agreement between whole blood, plasma, and serum was tested with 84 patient samples collected from an emergency room. Whole blood was collected into a heparinized tube; plasma was prepared from half this sample. Serum was collected in a tube without heparin. Twenty-two samples were positive for myoglobin and troponin I while 21 samples were positive for CK-MB. There was 100% agreement between the sample types.

3. Clinical studies:

a. Clinical Sensitivity:

See method comparison data above.

b. Clinical specificity:

See method comparison data above.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

The tests are designed to yield a positive result when concentrations are: ≥ 0.6 ng/mL for troponin I, ≥ 70 ng/mL for myoglobin, and ≥ 5 ng/mL for CK-MB.

5. Expected values/Reference range:

Not applicable. This is a qualitative assay.

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.