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

A. 510(k) Number:
k063756

B. Purpose for Submission:
New device

C. Measurand:
Cardiac troponin I

D. Type of Test:
Two-site sandwich immunoassay, quantitative

E. Applicant:
Dade Behring Inc.

F. Proprietary and Established Names:
Dimension Vista™ CTNI Flex® reagent cartridge

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 (Immunoassay method, troponin subunit)

4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See indications for use below.

2. Indication(s) for use:

   The CTNI method is an in vitro diagnostic test for the quantitative measurement of cardiac troponin I in human serum and plasma on the Dimension Vista system. Measurements of cardiac troponin I are used to aid in the diagnosis of acute

myocardial infarction (AMI) and in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality.

3. Special conditions for use statement(s):
   For prescription use

4. Special instrument requirements:
   Dade Behring Dimension Vista system

I. Device Description:

The Dimension Vista CTNI Flex reagent cartridge consists of two latex bead reagents and a reagent containing a biotinylated anti-cardiac troponin I mouse monoclonal antibody fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a second anti-cardiac troponin I mouse monoclonal antibody and contains chemiluminescent dye.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dade Behring Dimension CTNI immunoassay

2. Predicate 510(k) number(s):
   k010313

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	For the quantitative measurement of cardiac troponin I in human serum. Measurements of cardiac troponin I are used to aid in the diagnosis of acute myocardial infarction (AMI) and in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality	For the quantitative measurement of cardiac troponin I in human serum and plasma. Measurements of cardiac troponin I are used to aid in the diagnosis of acute myocardial infarction (AMI) and in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality
Sample type	Serum and heparinized plasma	Serum and heparinized plasma

Differences		
Item	Device	Predicate
Assay type	Chemiluminescent immunoassay	Photometric immunoassay
Reportable range	0.015 to 40 ng/mL	0.04 to 40 ng/mL
Limit of Quantitation (Functional Sensitivity)	0.04 ng/mL	Not specified
Sample volume	20 µL	50 µL

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

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition (CLSI EP5-A2)
- Interference Testing in Clinical Chemistry; Approved Guideline (CLSI EP7-A2)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition (CLSI EP9-A2)

Also referenced: Dade Behring Dimension Vista™ CTNI Flex® reagent cartridge; Dimension Vista™ CTNI Calibrator; Dimension Vista™ CTNI SDIL Sample Diluent premarket notification k053577

L. Test Principle:

The Dimension Vista CTNI method is a one-step sandwich chemiluminescent immunoassay based on Luminescent Oxygen Channeling Immunoassay (LOCI) technology. The LOCI reagents consists of two latex bead reagents and a reagent containing a biotinylated anti-cardiac troponin I monoclonal antibody fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a second anti-cardiac troponin I monoclonal antibody and contains chemiluminescent dye. The sample is incubated with Chemibeads and biotinylated antibody to form a particle/cardiac troponin I/biotinylated antibody sandwich. Sensibeads are then added and bind to the biotin to form bead-aggregated immunocomplexes. Illumination of the complex by light at 680 nm generates singlet oxygen from Sensibeads, which diffuses into the Chemibeads and triggers a chemiluminescent reaction. The resulting chemiluminescent signal is measured at 612 nm and is a direct function of the cardiac troponin concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   The precision study was performed over a period of 20 days following the CLSI EP5-A2 guideline and included four serum pools with TnI at 4 different levels (0.07, 0.43, 22.5 and 30.6 ng/mL) and one commercial control. Repeatability ranged from 1.0-3.8% CV and within lab imprecision ranged from 1.05-7.36% CV.

   Limit of Quantitation was evaluated by determining the total imprecision of serum samples with levels of TnI ranging from 0.033 to 0.16 ng/mL. Two replicates of each sample were tested once per day for 20 days. The limit of quantitation was determined to be 0.04 ng/mL and corresponds to a coefficient of variation (CV) of 10%.

   b. *Linearity/assay reportable range:*
   The reportable range of the assay is 0.015 to 40 ng/mL.

   Linearity was evaluated by comparing the observed versus expected values obtained with the Dimension Vista CTNI method. Two natural troponin I samples, one serum and one heparinized plasma, at TnI concentrations approximately 45 ng/mL, were mixed with Sample Diluent in different proportions across the range of the assay. Test sample TnI concentrations ranged from 4 to 34 ng/mL. The observed results recovered in the range of 98-105% of the expected TnI values.

   High dose hook effect was evaluated by testing normal human sera spiked with troponin I at high concentrations up to 1010 ng/mL. No hook effect was observed with samples up to this level.

   The Dimension Vista system will report an error code to the user when the signal generated by high level TnI samples exceeds 40 ng/mL. The labeling states that samples above 40 ng/mL may be manually diluted with Sample Diluent at no greater than a 1:5 ratio and retested. Dilution was reviewed previously under k053577.

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   Not applicable.

   d. *Detection limit:*
   The analytical sensitivity was defined as the concentration corresponding to two standard deviations above the mean of a sample containing no troponin I (n=20). Twenty replicates of the Dimension Vista CTNI calibrator Level A (0 ng/mL) were evaluated in the CTNI assay and resulted in an analytical sensitivity ~0.015 ng/mL.

The Limit of Quantitation is 0.04 ng/mL (see precision section above).

e. Analytical specificity:
Evaluation of analytical specificity (cross-reactivity) was done by first spiking each cross-reactant to target concentration into a serum sample. Then, a control for each cross-reactant was prepared by spiking the samples with the same volume of the solvent used for reconstituting the cross-reactant. The cross-reactant test samples and the control samples were measured on the Dimension Vista and the cross-reactivity was calculated.

Cross-reactant	**Concentration**	**% Cross-reactivity**
Troponin-C (cardiac)	1000 ng/mL	None
Troponin-T (cardiac human)	1000 ng/mL	0.05
Troponin-I (skeletal human)	1000 ng/mL	0.14
Troponin-I (skeletal human)	280 ng/mL	0.11

The sponsor followed the CLSI EP7-A2 guideline for interference testing. The sponsor defined interference as a difference in recovery between the test sample and control greater than 10%. Hemoglobin hemolysate (up to 500 mg/dL), conjugated and unconjugated bilirubin (up to 60 mg/dL), and lipid (up to 3000 mg/dL) did not interfere with the test.

A panel of commonly ingested substances, over-the-counter drugs and cardiac drugs did not interfere with the assay. This claim was previously reviewed under k053577.

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. Method comparison with predicate device:
Serum samples were tested on the Dade Behring Dimension Vista CTNI and the Dimension RxL test system using CLSI EP9-A2 as a guide. Deming regression was used for the analysis.

Mean values of duplicate samples were used for both methods. Since the AMI cut-off of the device is stated to be 0.6-1.5 ng/mL, performance at the lower, medically significant part of the assay range (TnI < 10 ng/mL) was characterized in addition to the full assay range. The following table shows regression coefficient estimates along with their 95% confidence intervals.

Analysis (N)	Sample range (ng/mL) (N)	Intercept (β_0)	95% CI (β_0)	Slope (β)	95% CI (β)
All samples	0.02-38.9 (90)	-0.1416	(-0.48, 0.20)	1.024	(0.991, 1.057)
TnI < 10 ng/mL	0.02-10 (71)	0.0067	(-0.17, 0.18)	0.993	(0.943, 1.043)

The following percent (%) agreement tables compare 92 results of the Dimension RxL TnI assay with the current Dimension Vista TnI assay qualitatively with three TnI cut-off concentrations of 0.6, 1.0 and 1.5 ng/mL. The data is presented below for each cut-off concentration.

Cut-off at 0.6

		Dimension RxL		
		>= **0.6**	< **0.6**	Total
Vista	>= **0.6**	77	0	77
	< **0.6**	0	15	15
	Total	77	15	92

Positive % agreement: 100% (77/77) 95% CI: (95.3%; 100%)
Negative % agreement: 100% (15/15) 95% CI: (78.2%; 100%)

Cut-off at 1.0

		Dimension RxL		
		>= **1.0**	< **1.0**	Total
Vista	>= **1.0**	74	1	75
	< **1.0**	1	16	17
	Total	75	17	92

Positive % agreement: 98.7% (74/75) 95% CI: (92.8%; 99.9%)
Negative % agreement: 94.1% (16/17) 95% CI: (71.3%; 99.9%)

Cut-off at 1.0

		Dimension RxL		
		>= **1.5**	< **1.5**	Total
Vista	>= **1.5**	63	1	64
	< **1.5**	2	26	28
	Total	65	27	92

Positive % agreement: 96.9% (63/65)	95% CI: (89.3%; 99.6%)
Negative % agreement: 96.3% (26/27)	95% CI: (81%; 99.9%)

b. Matrix comparison:

The sponsor demonstrated equivalence between serum and heparinized plasma by method comparison of sixty-three (63) matched sample sets on the Dimension Vista CTNI method. The samples ranged in TnI value from approximately 0.026 to 24 ng/mL. Analysis by linear least squares regression yielded the following equation:

y (lithium heparin plasma)= 1.02x (serum) + 0.031; r=0.999

Equivalence between lithium and sodium heparinized plasma was demonstrated by method comparison of fifty (50) matched sample sets on the Dimension Vista CTNI method. The samples ranged in TnI value from approximately 0.1 to 38 ng/mL. Analysis by linear least squares regression yielded the following equation:

y (sodium heparin)= 0.99x (lithium heparin) - 0.05; r=0.998

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:

A cut-off range of 0.6-1.5 ng/mL was established for the Dade Behring Stratus Cardiac TnI assay in k951890. A previous method comparison study (k973650) with the Cardiac Troponin I method for the Dimension RxL demonstrated substantial equivalence of that assay to the Stratus Cardiac TnI assay. A method comparison of the current device to Dimension RxL was performed to support the current Dimension Vista TnI assay (see method comparison section 2(a) above).

5. Expected values/Reference range:
In a study of 150 matched serum and plasma samples from apparently healthy individuals, the upper limit of the 99th percentile for the Dimension VISTA™ CTNI method was determined to be approximately 0.04 ng/mL for both matrices.

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.