

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

A. 510(k) Number:

k053577

B. Purpose for Submission:

New device

New calibrator

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

Dimension Vista™ CTNI Calibrator

Dimension Vista™ CTNI SDIL Sample Diluent

G. Regulatory Information:

1. Regulation section:

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

21 CFR 862.1150, Calibrator

2. Classification:

Class II

3. Product code:

MMI (Immunoassay method, troponin subunit)

JIT (Calibrator, secondary)

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 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.

The CTNI CAL is an in vitro diagnostic product for the calibration of cardiac troponin I on the Dimension Vista system.

The CTNI SDIL is for use on the Dimension Vista system to dilute samples with elevated CTNI results.

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 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 Dimension CTNI calibrator is supplied as a frozen, liquid product. It is human serum based and contains troponin complex, stabilizers, and preservative. It is packaged in six vials: 2 vials Calibrator A (2 mL each), 2 vials Calibrator B (1 mL each) and 2 vials Calibrator C (1.5 mL each).

CTNI sample diluent is supplied as 6 vials, each containing 2.5 mL. It is a liquid, human serum based product with stabilizers and preservative.

Human source material was tested and found negative for HIV-1/2, HBsAg, and HCV by FDA-approved methods.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dade Behring Dimension CTNI immunoassay
Dade Behring Dimension CTNI calibrator

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

k010313, k010314

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

Differences		
Item	Device	Predicate
Assay type	Chemiluminescent immunoassay	Photometric immunoassay
Sample type	Serum	Serum and plasma
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)

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition (CLSI EP9-A2)

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 a protocol similar to CLSI EP5-A2 and included commercial controls as well as normal human sera spiked with TnI at 3 different levels (0.12, 0.55, and 31.4 ng/mL). Repeatability ranged from 1.5-5.8% CV and within lab imprecision ranged from 2.9-6.6% CV.

Limit of Quantitation (Functional Sensitivity) was evaluated by determining the total imprecision of natural TnI samples. 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. A high concentration natural troponin I sample was mixed with a normal serum in different proportions across the range of the assay. The observed results recovered in the range of 95-99.9% 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 1280 ng/mL. No hook effect was observed with samples up to this level.

Accurate dilution of samples using Dimension Vista SDIL CTNI sample diluent was demonstrated by diluting multiple elevated samples (17-40

ng/mL), at a 1:5 ratio. The sponsor determined the results to be acceptable if recovery was within 10% of the expected value and all diluted samples met this criterion.

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.

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

Traceability and Value Assignment:

Dimension Vista CTNI calibrators are traceable to Primary Reference Calibrators that are prepared from native human sera and assigned values using the Dade Behring Stratus® CS system. Manufacturers Working Calibrators (Master Pools) are prepared from a normal human serum pool spiked with human troponin complex. Their value is measured from the Primary Reference Calibrators tested on the Dimension Vista system, using several instruments and reagent lots. The Master Pool value is assigned from the mean of all test results.

The commercially available Dimension Vista CTNI calibrators consist of troponin complex spiked into troponin I negative serum pool at three levels of TnI. The values of these calibrators are measured from the Master Pool calibrators tested on the Dimension Vista CTNI system, using several instruments and reagent lots. The calibrator value is assigned for each of the three levels from the mean of all test results.

Stability: The shelf life of the product is stated to be 12 months when stored frozen between -10°C and -20°C. The calibrators are stable for 7 days, once thawed if stored unopened at 2-8°C or opened and re-capped immediately. The thawed calibrator is also stable for 7 days when stored on-board the Dimension Vista system, once the stopper of the vial is punctured.

Stability studies were performed to support these claims. The sponsor's acceptance criterion was that value at each testing point should recover within 5% of the assigned bottle value.

Stability studies for the CTNI Sample Diluent were performed to support the claim of 12 months for the unopened product when stored at 2-8°C and the claim of 30 days for the opened product.

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 spiking each cross-reactant to target concentration into a troponin I negative serum as well as a serum spiked with human troponin complex to approximately 1.0 ng/mL. 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	0.06
Troponin-I (skeletal human)	1000 ng/mL	0.12
Troponin-I (skeletal human)	280 ng/mL	0.13

The effect of potentially interfering substances, including endogenous substances, commonly ingested substances and cardiac drugs were tested by spiking a sample containing approximately 1 ng/mL TnI with the appropriate concentration of the test substance and comparing the TnI recovery of the sample to that of a control sample. The control sample was prepared by spiking the TnI sample with an equal volume of the solvent used to dissolve the test substance. 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 40 mg/dL), lipid (up to 3000 mg/dL), and cholesterol (up to 500 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. A list of these substances can be found in the package insert.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Serum samples were tested on the Dimension Vista CTNI and the Dade Behring Dimension RxL test system following a protocol similar to CLSI EP9-A2. The method used to fit the linear regression line was ordinary least squares.

Comparative Method	Slope	Intercept ng/mL [µg/L]	Correlation Coefficient	Sample Range ng/mL [µg/L]	n
Dimension® RxL System	1.015	-0.003	0.993	0.015- 35.72	197

The following percent (%) agreement tables compare results of the Dimension RxL TnI assay with the current Dimension Vista TnI assay qualitatively versus three TnI concentrations ranging from 0.6 to 1.5 ng/mL.

Qualitative comparison at 0.6 ng/mL

		Dimension RxL		
		>= 0.6	< 0.6	Total
Vista	>= 0.6	106	1	107
	< 0.6	0	91	91
	Total	106	92	198

Positive % agreement: 100% (106/106) 95% CI: (96.6%, 100%)

Negative % agreement: 98.9% (91/92) 95% CI: (94.1%, 99.9%)

Qualitative comparison at 1.0 ng/mL

		Dimension RxL		
		>= 1.0	< 1.0	Total
Vista	>= 1.0	99	0	99
	< 1.0	1	98	99
	Total	100	98	198

Positive % agreement: 99% (99/100) 95% CI: (94.6%, 99.9%)

Negative % agreement: 100% (98/98) 95% CI: (96.3%, 100%)

Qualitative comparison at 1.5 ng/mL

		Dimension RxL		
		>= 1.5	< 1.5	Total
Vista	>= 1.5	85	2	87
	< 1.5	1	110	111
	Total	86	112	198

Positive % agreement: 98.8% (85/86) 95% CI: (93.7%, 99.9%)

Negative % agreement: 98.2% (110/112) 95% CI: (93.7%, 99.8%)

- b. Matrix comparison:*
Not applicable

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 above).

5. Expected values/Reference range:

In a study of 199 serum samples from apparently healthy individuals, the upper limit of the 99th percentile for the Dimension VISTA™ CTNI method was determined to be 0.045 ng/mL.

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.