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

A. 510(k) Number:
K031031

B. Analyte:
Troponin I

C. Type of Test:
Quantitative immunometric assay

D. Applicant:
Ortho-Clinical Diagnosics, Inc.

E. Proprietary and Established Names:
Vitros Immunodiagnostic Products Troponin I Reagent Pack
Vitros Immunodiagnostic Products Troponin I Calibrators

F. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1215, Creatine Phosphokinase/Creatine Kinase or Isoenzymes Test System
   862.1150, Calibrator
2. Classification:
   Class II
3. Product Code:
   MMI, JIT
4. Panel:
   Clinical Chemistry

G. Intended Use:

1. Indication(s) for use:
   For the *in vitro* quantitative measurement of Troponin I (cTnI) in human heparin plasma to aid in the diagnosis of myocardial infarction.

   For use in the calibration of the *Vitros* Immunodiagnostic System for the quantitative measurement of cardiac Troponin I (cTnI) in human heparin plasma.

2. Special condition for use statement(s):
   For *in vitro* diagnostic use only.

   For prescription use by laboratories only.

3. Special instrument Requirements:
   Vitros ECi Immunodiagnostic System with Intellicheck™

H. Device Description:

The Vitros Immunodiagnostic products Troponin I Reagent Pack and calibrators is designed to measure cardiac Troponin I (cTnI) concentration in heparin plasma using the Vitros ECi System. The device consists of streptavidin-coated plates and two other wet reagents including antibodies (biotinylated mouse monoclonal anti-cTnI antibody and horseradish peroxidase (HRP)-labeled goat polyclonal anti-cTnI antibody) and a light-producing indicator.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Vitros Immunodiagnostic Products Troponin I Reagent Pack
   Dade Dimension™ RxL Cardiac Troponin I (TROP) Method
2. Predicate K number(s):
   K020662
   K973650
3. Comparison with predicate:

   This submission is to bring about changes in the labeling of a marketed product. The device is identical to the predicate in all ways except those indicated below:

   Changes in wording to reflect revised standardized wording related to reagent handling and specimen collection and preparation. The sponsor adds more specific language to indicate the same instructions.

   Additional statements were added to the Limitations of Procedure section to emphasize the effect that heterophilic antibody may have on the assay.

   Additional performance testing was done to determine the extent of hemoglobin interference on specimens containing low levels of Troponin I, and this information was added to the labeling.

   Additional performance testing was done to determine the low concentration precision. Data defining imprecision at the upper reference limit, the AMI cutoff, and the lowest concentration with a 10% CV was added to the labeling.

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

K. Test Principle:

Troponin I (cTnI) present in the sample reacts simultaneously with biotinylated mouse monoclonal anti-cTnI antibody and horseradish peroxidase (HRP)-labeled goat polyclonal anti-cTnI antibody (affinity purified). The Troponin-antibody complex is captured by streptavidin which coats the sample wells and unbound material is washed away. Signal reagent is added which contains a luminal derivative and a peracid salt as well as a signal enhancer (substituted acetanilide). HRP catalyzes the oxidation of the luminal derivative producing light (the signal enhancer increases the

level and duration of the light). This signal can be detected by the VITROS ECi System, allowing the determination of the concentration of HRP in the well. The amount of bound HRP is directly proportional to the concentration of cTnI in the sample.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Additional performance testing was done to determine the low concentration precision.

Precision was evaluated at cTnl concentrations equal to, and below the AMI cutoff of 0.4 ng/mL (µg/L). Ten patient sample pools were assayed once per day on 11 days over a 28 day period using a single reagent lot. Calibration was performed at the initiation of the data collection period. The precision profile was constructed using all of the pools above the analytical sensitivity. The data presented are provided as a guideline.

The SD observed at the URL of 0.08 ng/mL (µg/L) and at the AMI Cutoff of 0.4 ng/mL (µg/L) were 0.010 (12.0 %CV) and 0.024 (5.9% CV) ng/mL (µg/L), respectively. The lowest concentration at which the VITROS Troponin I assay achieved a 10% CV was 0.12 ng/mL (µg/L).

	cTnI	**Inter-assay Precision**	
	ng/mL	**SD**	**CV%**
Upper Reference Limit (URL)	0.08	0.010	12.0
Lowest Concentration with 10% CV	0.12	0.012	10.0
AMI Cutoff	0.40	0.024	5.9

b. Linearity/assay reportable range:

Not addressed in this submission.

c. Traceability (controls, calibrators, or method):

No changes were made to the calibrators or the method. In addition, the calibrators were not impacted by the labeling changes in this submission.

d. Detection limit:

Not addressed in this submission.

e. Analytical specificity:

This additional statement was added to the Limitations of Procedure section to emphasize the effect that heterophilic antibody may have on the assay:

Persistently elevated cTnI results may be due to the presence of heterophilic antibodies, such as anti-mouse antibodies (HAMA) and to nonspecific protein binding.

- Heterophilic antibodies in samples can cause interference with immunoassays. Although the prevalence of heterophilic antibodies is unknown, a recent report estimates they are present in 3.4% of healthy individuals. Heterophilic antibodies may be present in blood samples from individuals who have been regularly exposed to animals or treated therapeutically with animal proteins. The impact of heterophilic antibodies as an interferent is dependent on the extent of an individual's exposure to animals or animal proteins and the characteristics of the immunoassay. A set of dilutions of human anti-mouse antibody (HAMA) in a normal serum pool gave apparent cTnI concentrations less than 0.05 ng/mL (µg/L) in the presence of HAMA concentrations up to 2,976 ng/mL.
- Interpretation of cTnI results should be done only in the context of the overall clinical picture, e.g., clinical history, ECG, and other laboratory tests indicative of cardiac damage such as CKMB, CK, or myoglobin. The triage of patients with chest pain should be based on serial samples and the typical rise and fall pattern of cTnI characteristic of cardiac damage.

Additional performance testing was done to determine the extent of hemoglobin interference on specimens containing low levels of Troponin I, and this information was added to the labeling. (as below)

Interference was evaluated as recommended by NCCLS Protocol EP7. Hemoglobin may interfere with the Vitros Troponin I assay.

At a cTnI level of 0.026 ng/mL, hemoglobin at 100, 250, and 500 mg/dL caused a positive bias of 0.043, 0.175 and 0.226 ng/mL respectively. At a cTnI level of approximately 0.3 ng/mL, hemoglobin at 100, 250 and 500 mg/dL caused a positive bias of 0.029, 0.075 and 0.166 ng/mL respectively.

Interferent	Interferent Concentration		Units = ng/mL (μg/L)	
			Analyte Conc.*	Bias**
Hemoglobin	0.062 mmol/L	100 mg/dL	0.026	0.043
Hemoglobin	0.155 mmol/L	250 mg/dL	0.026	0.175
Hemoglobin	0.310 mmol/L	500 mg/dL	0.026	0.226
Hemoglobin	0.062 mmol/L	100 mg/dL	0.279	0.029
Hemoglobin	0.155 mmol/L	250 mg/dL	0.305	0.075
Hemoglobin	0.310 mmol/L	500 mg/dL	0.347	0.166

* Average test concentration of replicate determinations using one or two different lots of reagent.
** Estimate of the average difference observed

f. Assay cut-off:

See precision above for information on upper reference limit imprecision.

2. Comparison studies:
   a. Method comparison with predicate device:

   Not applicable.

   b. Matrix comparison:

   Not addressed in this submission.

3. Clinical studies:
   a. Clinical sensitivity:

   Not addressed in this submission.

   b. Clinical specificity:

   Not addressed in this submission.

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

4. Clinical cut-off:

Not addressed in this submission.

The labeling states that the recommended AMI cutoff is 0.4 ng/mL for heparin plasma. This cutoff was determined by comparing clinically diagnosed AMI patients to clinically diagnosed non-AMI patients. Of the 267 chest pain patients enrolled in this study, 40

were diagnosed with AMI and 227 were diagnosed non-AMI. These data were analyzed by Receiver Operator Characteristic (ROC) curve analysis to characterize the diagnostic cutoffs for AMI. Testing was performed using one System and seven reagent lots

5. Expected values/Reference range:

The URL is 0.08 ng/mL (µg/L) based on a panel of 798 fresh heparin plasma samples from normal blood donors between the ages of 18-89 years (61.3% male donors and 38.7% female donors collected across six sites). The observed value for the upper 99 th percentile is 0.06 ng/mL (µg/L) with a 90% confidence interval of 0.05-0.08 ng/mL (µg/L). The URL represents the upper limit of the 90% confidence interval of the 99th percentile. The observed value for the upper 97.5 percentile is 0.04 ng/mL (µg/L) with a 90% confidence interval of 0.03-0.05 ng/mL (µg/L). Testing was performed using six Systems and four reagent lots.

M. Conclusion:

I recommend that the *Vitros* Immunodiagnostic Products Troponin I Reagent Pack and *Vitros* Immunodiagnostic Products Troponin I Calibrators is substantially equivalent to the legally marketed predicate device.