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

A. 510(k) Number:

k082699

B. Purpose for Submission:

New device

C. Measurand:

Troponin I

D. Type of Test:

Quantitative immunoassay

E. Applicant:

Roche Diagnostics, Inc.

F. Proprietary and Established Names:

Elecsys Troponin I Immunoassay

Elecsys Troponin I STAT Immunoassay

Elecsys PreciControl Troponin

Elecsys Troponin I CalSet

Elecsys Troponin I STAT CalSet

G. Regulatory Information:

1. Regulation section:

Device	Regulation	Classification	Product Code
Elecsys Troponin I	21 CFR § 862.1215	II	MMI
Elecsys Troponin I STAT	21 CFR § 862.1215	II	MMI
Elecsys PreciControl Troponin	21 CFR § 862.1660	I, reserved	JJY
Elecsys Troponin I CalSet	21 CFR § 862.1150	II	JIT
Elecsys Troponin I STAT CalSet	21 CFR § 862.1150	II	JIT

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   Elecsys Troponin I Immunoassay: Immunoassay for the in vitro quantitative determination of cardiac troponin I in human serum and plasma. The Elecsys Troponin I assay is intended to aid in the diagnosis of myocardial infarction. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Elecsys and MODULAR Analytics E170 immunoassay analyzers.

   Elecsys Troponin I STAT Immunoassay: Immunoassay for the in vitro quantitative determination of cardiac troponin I in human serum and plasma. The Elecsys Troponin I STAT assay is intended to aid in the diagnosis of myocardial infarction. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Elecsys analyzers.

   Elecsys PreciControl Troponin: The Elecsys PreciControl Troponin I used for quality control of the Elecsys Troponin I and Elecsys Troponin I STAT immunoassays on the Elecsys and MODULAR Analytics E170 Analyzers.

   Elecsys Troponin I CalSet: The Elecsys Troponin I CalSet is used for calibrating the quantitative Elecsys Troponin I assay on the MODULAR ANALYTICS E170 analyzers.

   Elecsys Troponin I STAT CalSet: The Elecsys Troponin I STAT CalSet is used for calibrating the quantitative Elecsys Troponin I STAT assay on the Elecsys analyzers.

3. Special conditions for use statement(s):

   Prescription use

4. Special instrument requirements:

   Roche Elecsys 2010 and Roche Modular Analytics E170

I. Device Description:

All reagents, controls and calibrators are sold separately.

a. Elecsys Troponin I Immunoassay and Elecsys Troponin I STAT Immunoassays: The Elecsys Troponin I and Troponin I STAT immunoassays are two step sandwich immunoassays with streptavidin microparticles and electrochemiluminescence detection. Results are determined using a calibration curve that is generated specifically on each instrument by a 2 point calibration and a master curve provided with the reagent bar code. The Elecsys Troponin I STAT immunoassay is completed in half time when compared to the Elecsys Troponin I immunoassay, however the composition of the reagents is identical.

b. Elecsys PreciControl Troponin: The Elecsys PreciControl Troponin is a lyophilized product consisting of human serum containing Troponin I in two concentration ranges and Troponin T. Although the control contains both Troponin subunits, only the Troponin I has assayed values. This material is not for use with Troponin T assays. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

c. Elecsys Troponin I CalSet and Elecsys Troponin I STAT CalSet: The Elecsys Troponin I CalSet and Elecsys Troponin I STAT CalSet are lyophilized products consisting of human serum with added Troponin I in two concentration ranges. During manufacture the analyte is spiked into the matrix at the desired concentration levels. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 2. Predicate k number(s):

Device	Predicate k number	Predicate device name
Elecsys Troponin I	k021814	Beckman Coulter Access AccuTnI
Elecsys Troponin I STAT	k021814	Beckman Coulter Access AccuTnI

Elecsys PreciControl Troponin	k072437	Elecsys PreciControl Cardiac I
Elecsys Troponin I CalSet	k072437	Elecsys proBNP II CalSet
Elecsys Troponin I CalSet STAT	k072437	Elecsys proBNP II CalSet

3. Comparison with predicate:

Similarities – Elecsys Troponin I		
Item	Device	Predicate
Assay Protocol	Sandwich Principle	Same
Sample Type	Human serum and plasma	Same

Differences - Elecsys Troponin I		
Item	Device	Predicate
Intended Use / Indication for Use	Immunoassay for the in vitro quantitative determination of cardiac troponin I in human serum and plasma. The Elecsys Troponin I assay is intended to aid in the diagnosis of myocardial infarction. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Elecsys and MODULAR Analytics E170 immunoassay analyzers.	The Access AccuTnI assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and cardiac muscle damage. Cardiac troponin I determination aids in the risk stratification of patients with unstable angina or non-ST segment elevation acute coronary syndromes with respect to relative risk of mortality, myocardial infarction, or increased probability of ischemic events requiring urgent revascularization procedures.
Detection Protocol	Electrochemiluminescence	Chemiluminescence
Traceability/Standardization	Standardized against a commercially available Troponin I assay	Not stated.
Calibration Interval	Calibration must be	An active calibration curve is

Differences - Elecsys Troponin I		
Item	Device	Predicate
	performed once per reagent lot using fresh reagent. Renewed calibration: • After 1 month (28 days) when using the same reagent lot • After 7 days (when using the same reagent kit on the analyzer)	required for all tests. For the Access AccuTnI assay, calibration is required every 56 days.
Reagent Stability	Unopened • Up to stated expiration date stored at 2-8ºC After Opening • 4 weeks at 2-8ºC • 4 weeks on the analyzers	Unopened • Up to stated expiration date stored at 2-8ºC After Opening • Stable at 2 – 10°C for 56 days after initial use
Calibrator	Elecsys Troponin I STAT CalSet	Access AccuTnI Calibrators
Controls	Elecsys PreciControl Troponin	Commercial control material
Instrument	Modular Analytics E170	Access Immunoassay Systems
Expected values	Age 20 – 79, expected value < 0.3 ng/mL: Values less than 0.3 ng/mL will be reported as "< 0.3 ng/mL".	Age 19 – 88: 97.5th percentile: 0.03 ng/mL 99th percentile: 0.04 ng/mL
Measuring Range	0.3-25.00 ng/mL	0.01 – 100 mcg/L (ng/mL)
Cut-off	0.3 ng/mL	0.5 ng/mL
No Hook Effect up to	1000 ng/mL	1,920 ng/mL
Limit of Blank	Studies performed and LoB is less than LoQ (0.3 ng/mL)	Not given
Limit of Detection	Studies performed and LoB is less than LoQ (0.3 ng/mL)	0.01 ng/mL (LDL)
Limit of Quantitation	0.3 ng/mL at 10% CV	0.03 ng/mL at 20% CV 0.06 ng/mL at 10% CV

Similarities - Elecsys Troponin I STAT

Item	Device	Predicate
Assay Protocol	Sandwich Principle	Same
Detection Protocol	Electrochemiluminescence	Same
Sample Type	Human serum and plasma	Same

Differences - Elecsys Troponin I STAT		
Item	Device	Predicate
Intended Use / Indication for Use	Immunoassay for the in vitro quantitative determination of cardiac troponin I in human serum and plasma. The Elecsys Troponin I STAT assay is intended to aid in the diagnosis of myocardial infarction. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Elecsys analyzers.	The Access AccuTnI assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and cardiac muscle damage. Cardiac troponin I determination aids in the risk stratification of patients with unstable angina or non-ST segment elevation acute coronary syndromes with respect to relative risk of mortality, myocardial infarction, or increased probability of ischemic events requiring urgent revascularization procedures.
Calibration Interval	Calibration must be performed once per reagent lot using fresh reagent. Renewed calibration: • After 1 month (28 days) when using the same reagent lot • After 7 days (when using the same reagent kit on the analyzer)	An active calibration curve is required for all tests. For the Access AccuTnI assay, calibration is required every 56 days.
Reagent Stability	Unopened • Up to stated expiration date stored at 2-8ºC After Opening • 4 weeks at 2-8ºC • 4 weeks on the	Unopened • Up to stated expiration date stored at 2-8ºC After Opening • Stable at 2 – 10°C for 56 days after initial use

Differences - Elecsys Troponin I STAT		
Item	Device	Predicate
	analyzers	
Calibrator	Elecsys Troponin I STAT CalSet	Access AccuTnI Calibrators
Controls	Elecsys PreciControl Troponin	Commercial control material
Instrument	Elecsys 2010	Access Immunoassay Systems
Expected values	Age 20 – 79, expected value < 0.3 ng/mL: Values less than 0.3 ng/mL will be reported as "< 0.3 ng/mL".	Age 19 – 88: 97.5th percentile: 0.03 ng/mL 99th percentile: 0.04 ng/mL
Measuring Range	0.3-25.00 mcg/L (ng/mL)	0.01 – 100 mcg/L (ng/mL)
Cut-off	0.3 ng/mL	0.5 ng/mL
No Hook Effect up to	1,000 ng/mL	1,920 ng/mL
Limit of Blank	Studies performed and LoB is less than LoQ (0.3 ng/mL)	Not given
Limit of Detection	Studies performed and LoB is less than LoQ (0.3 ng/mL)	0.01 ng/mL (LDL)
Limit of Quantitation Functional Sensitivity	0.3 ng/mL at 10% CV	0.03 ng/mL at 20% CV 0.06 ng/mL at 10% CV

Similarities - Elecsys PreciControl Troponin

Item	Device	Predicate
Levels	Two	Same
Format	Lyophilized, based on human serum	Same
Freeze-thaw stability	After thawing- use only once	Same
Reconstituted volume	2 mL	Same

Differences – Elecsys PreciControl Troponin		
Item	Device	Predicate
Intended Use	Used for quality control of the Elecsys Troponin I and Elecsys Troponin I STAT immunoassays on the Elecsys and MODULAR Analytics E170 Analyzers.	Used for quality control of specified immunoassays on the elecsys and **cobas e** immunoassay analyzers
Analyte Constituents	Troponin T and Troponin I	CK-MB, Digitoxin, Myoglobin, NT-proBNP

Differences – Elecsys PreciControl Troponin		
Item	Device	Predicate
Reconstituted Stability	5 hrs at 20-25°C 4 days at 2-8°C 3 months at -20°C (freeze only once)	3 hrs at 20-25°C 3 days at 2-8°C 3 months at -20°C (freeze only once)

Similarities - Elecsys Troponin I CalSet		
Item	Device	Predicate
Levels	Two	Same
Freeze-thaw stability	After thawing- use only once	Same
Reconstituted volume	1 mL	Same

Differences - Elecsys Troponin I CalSet		
Item	Device	Predicate
Intended Use	Used for calibrating the quantitative Elecsys Troponin I assay on the Elecsys and MODULAR ANALYTICS E170 analyzers.	Used for calibrating the quantitative elecsys proBNP II assay on elecsys and **cobas e** immunoassay analyzers.
Format	Lyophilized, based on human serum	Lyophilized, based on equine serum
Analyte Constituents	Troponin I	CK-MB, Digitoxin, Myoglobin, NT-proBNP

Similarities - Elecsys Troponin I CalSet STAT		
Item	Device	Predicate
Levels	Two	Same
Freeze-thaw stability	After thawing- use only once	Same
Reconstituted volume	1 mL	Same

Differences - Elecsys Troponin I CalSet STAT		
Item	Device	Predicate
Intended Use	Used for calibrating the quantitative Elecsys Troponin I STAT assay on the Elecsys analyzers.	Used for calibrating the quantitative elecsys proBNP II assay on elecsys and **cobas e** immunoassay analyzers.
Format	Lyophilized, based on human serum	Lyophilized, based on equine serum
Analyte Constituents	Troponin I	CK-MB, Digitoxin,

Differences - Elecsys Troponin I CalSet STAT		
Item	Device	Predicate
		Myoglobin, NT-proBNP

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

CLSI EP5-A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline, 2nd ed

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples

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

L. Test Principle:

The Elecsys Troponin I Immunoassay and Elecsys Troponin I STAT Immunoassays use a sandwich principle for measurement of troponin I in serum or plasma. Two biotinylated monoclonal cardiac troponin I-specific antibodies labeled with a ruthenium complex react to form a sandwich complex during the first incubation period. Then, streptavidin-coated microparticles are added resulting in the binding of the complex to the solid phase via interaction of biotin and streptavidin. This occurs during a second incubation phase. Once this incubation is completed, the reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with a wash. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (5-point calibration) provided via the reagent barcode. The differences between the Elecsys Troponin I Immunoassay and Elecsys Troponin I STAT Immunoassays are that the STAT assay is completed in half the time as the other assay and is limited to use on specific analyzers.

The PreciControl Troponin contains two concentrations of troponin I and is used for monitoring the accuracy and precision of the Elecsys Troponin I and Elecsys Troponin I STAT immunoassays.

The Elecsys Troponin I CalSet and STAT CalSet are calibrators containing two concentrations of troponin I. All calibration information is included on a barcoded card which is loaded into the respective instrument systems.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

Elecsys Troponin I immunoassay and Elecsys Troponin I STAT:

Precision was evaluated using multiple serum or plasma pools. Samples were analyzed at a total of six laboratories within the US and outside of the US. Some laboratories had duplicate instrumentation and precision was performed on both analyzers. Samples were assayed in duplicate with a minimum of two runs per day using one reagent lot. Several sites did separate runs of serum and/or human plasma (HP) or had duplicate instrumentation indicated by #. The low control was also evaluated on both analyzers. The sponsor is using 0.3 ng/mL as the low limit of the measuring range based on precision of ≤ 10% CV at that value.

Troponin I STAT on e2010	**n**	**Concentration (ng/mL)**	**CV %**
Site			
1	63	0.323	8.8
2 #2	84	0.329	5.6
3 #2	63	0.347	7.9
Troponin 18 Minute on E170	**n**	**Concentration (ng/mL)**	**CV %**
Site			
5 #2	63	0.319	6.8
Troponin Control 1 on 2010 and E170	**n**	**Concentration (ng/mL)**	**CV %**
Site/Instrument/Assay			
2 2010,STAT	84	0.376	5.3
3 2010, STAT	63	0.395	4.7
4 2010, STAT	63	0.384	6.7
6 E170, 18 Min	63	0.322	5.6
5 E170, 18 Min	63	0.324	6.2

Additional precision studies were conducted for samples up to 18.0 ng/mL for both the Troponin I STAT and Troponin I immunoassays at US and non-US sites. Results are summarized are below:

Elecsys Troponin I STAT Assay	Elecsys Troponin I STAT Assay	Elecsys Troponin I Assay
US Site 1 Repeatability 4.8% CV @ 0.323 ng/mL 3.3% CV @ 0.496 ng/mL 2.2% CV @ 0.627 ng/mL 1.7% CV @ 21.400 ng/mL 4.2% CV @ 0.439 ng/mL 2.9% CV @ 17.800 ng/mL Within-lab 8.9% CV @ 0.323 ng/mL 5.9% CV @ 0.496 ng/mL 5.3% CV @ 0.627 ng/mL 3.2% CV @ 21.400 ng/mL 6.7% CV @ 0.439 ng/mL 3.6% CV @ 17.800 ng/mL US Site 2 Repeatability 3.0% CV @ 0.483 ng/mL 3.9% CV @ 0.329 ng/mL 1.8% CV @ 2.180 ng/mL 2.1% CV @ 0.691 ng/mL 4.0% CV @ 0.376 ng/mL 2.3% CV @ 17.300 ng/mL Within-lab 4.0% CV @ 0.483 ng/mL 5.7% CV @ 0.329 ng/mL 2.4% CV @ 2.180 ng/mL 2.9% CV @ 0.691 ng/mL 5.3% CV @ 0.376 ng/mL 2.6% CV @ 17.300 ng/mL	EU Site 1 Repeatability 2.5% CV @ 0.447 ng/mL 4.1% CV @ 0.347 ng/mL 0.7% CV @ 7.600 ng/mL 3.1% CV @ 0.498 ng/mL 2.6% CV @ 0.395 ng/mL 0.6% CV @ 17.600 ng/mL Within-lab 6.1% CV @ 0.447 ng/mL 16.1% CV @ 0.190 ng/mL 8.0% CV @ 0.347 ng/mL 4.3% CV @ 7.600 ng/mL 5.4% CV @ 0.498 ng/mL 4.8% CV @ 0.395 ng/mL 1.9% CV @ 17.600 ng/mL	Repeatability 5.3% CV @ 0.322 ng/mL 5.2% CV @ 0.425 ng/mL 2.7% CV @ 17.6 ng/mL 7.0% CV @ 0.340 ng/mL 2.6% CV @ 18.0 ng/mL Within-lab 8.7% CV @ 0.322 ng/mL 7.3% CV @ 0.425 ng/mL 4.7% CV @ 17.6 ng/mL 8.0% CV @ 0.340 ng/mL 4.4% CV @ 18.0 ng/mL

b. Linearity/assay reportable range:

Elecsys Troponin I immunoassay: Linearity was evaluated on the Roche

MODULAR Analytics E170. Three separate dilution series were prepared from three separate serum pools. Each high pool was assayed multiple times to determine the mean value prior to dilution. The samples were analyzed in three separate runs. Only native samples were used for this study. Diluent was used for a troponin free sample. Each serum pool was serially diluted to make 10 different concentrations. Each dilution was tested in triplicate and the median value was compared to the expected value. Linearity and recoveries were calculated against the expected values after dilution using Passing-Bablock, linear, and Deming regressions. Troponin I concentrations covered the measuring range of the assay.

	Slope (95% CI)	Intercept (95% CI)	Correlation
Passing-Bablock	0.9798 (0.9682, 0.9884)	-0.0089 (-0.0271, 0.0205)	Tau = 0.9939
Linear Regression	0.9834 (0.9758, 0.9910)	-0.06843 (-0.1333, -0.0035)	r = 0.9994
Deming Regression	0.9838 (0.9762, 0.9914)	-0.0718 (-0.1367, -0.0069)	r = 0.9996

Elecsys Troponin I STAT immunoassay:

Linearity was evaluated on the Roche Elecsys 2010. Three separate serum pools were prepared and dilutions and analysis used the same process as for the Elecsys Troponin I reagent. Each high pool was assayed multiple times to determine the mean value prior to dilution. Only native samples were used for this study. Diluent was used for a troponin free sample. Troponin I concentrations covered the measuring range of the assay.

	Slope (95% CI)	Intercept (95% CI)	Correlation
Passing-Bablock	0.9848 (0.9759, 0.9954)	-0.0017 (-0.0533, 0.0238)	Tau= 0.9787
Linear Regression	0.9838 (0.9767, 0.9908)	-0.0131 (-0.0431, 0.0693)	r =0.9977
Deming Regression	0.9841 (0.9770, 0.9911)	-0.0109 (-0.0453, 0.0671)	r = 0.9997

The sponsor is claiming a measuring range for both assays of 0.30 – 25.0 ng/mL (mcg/L). Values above the measuring range are reported as > 25.0 ng/mL (mcg/L). Values < 0.3 ng/mL are reported as < 0.3 ng/mL.

High dose hook effect was evaluated by testing normal human sera spiked with troponin I at 1,070 ng/mL and 1,300 ng/mL. There was no hook effect observed up to 1,300 ng/mL, however the sponsor sets the hook effect claim at 1,000 ng/mL in the labeling.

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

Calibrators

Elecsys Troponin I CalSet and Elecsys Troponin I STAT CalSet are traceable master calibrators which are standardized against another commercially available troponin I assay. Master calibrator value assignment occurs after 2 independent series are analyzed on 4 reference instruments. New lots of Troponin I CalSet and Troponin I STAT CalSet are analyzed multiple times against the master calibrators on the appropriate platform. The target value for the calibrators is then calculated as the median of the determined values.

Controls

Elecsys PreciControl Troponin is traceable to analysis against the master calibrators on the aforementioned platforms using specific reagent lots and multiple runs per instrument. The target values for the controls are then calculated as the median of the determined values.

Stability

The calibrators and controls are lyophilized. After reconstitution, they are stable for on-board the instruments for 5 hours, four days after opening at 2-8° C and 3 months at -20°C. Controls and calibrators should only be thawed once.

On-board calibration stability was verified on the Elecsys 2010 and the MODULAR Analytics E170 by measuring troponin I recovery in controls and human serum samples. Calibration is recommended every 7 days if the kit is not consumed and every 4 weeks with the same reagent lot and the reagent pack is consumed within 7 days.

The stability protocols and acceptance criteria were reviewed and found to be acceptable.

d. *Detection limit:*

Limits of Blank (LoB) and Limits of Detection (LoD) for Elecsys Troponin I and Elecsys Troponin I STAT were evaluated using CLSI EP17-A guideline. Limits of Quantitation (LoQ) for the two devices were established by determining the concentration with corresponds to an inter-assay CV of 10%. Studies were performed on analytical platforms appropriate to the devices.

Elecsys Troponin I:

LoB was determined by analyzing 5 troponin I free human serum samples on

one MODULAR Analytics E170 in singlicate in 6 runs over four days. LoB is < 0.3 ng/mL however, the sponsor is using the LoQ, 0.3 ng/mL, as the lowest limit of the measuring range.

LoD was determined by analyzing 5 human sera containing low amounts of troponin I on one MODULAR Analytics E170 in singlicate in 6 runs over three days. LoD < 0.3 ng/mL however the sponsor is using the LoQ, 0.3 ng/mL, as the lowest limit of the measuring range.

LoQ was determined by analyzing 6 serum samples and two controls with concentrations ranging from 0.0251 ng/mL to 17.1026 ng/mL were tested in singlicate on one MODULAR Analytics E170 for 10 days. The concentration with an inter-assay ≤ 10% CV was 0.3 ng/mL. The sponsor is using the LoQ as the lowest limit of the measuring range.

Elecsys Troponin I STAT:

LoB was determined by analyzing 5 troponin I free human serum samples on two Elecsys 2010s in 6 runs over four days. LoB < 0.3 ng/mL. The sponsor is using the LoQ, 0.3 ng/mL, as the lowest limit of the measuring range.

LoD was determined by analyzing 5 human sera containing low amounts of troponin I on two Elecsys 2010s in 6 runs over three days. LoD < 0.3 ng/mL. The sponsor is using the LoQ, 0.3 ng/mL, as the lowest limit of the measuring range.

LoQ was determined by analyzing 10 serum samples and two controls with concentrations ranging from 0.0251 ng/mL to 17.1026 ng/mL were tested in singlicate on one Elecsys 2010 for 10 days. The concentration with an inter-assay ≤ 10% CV was 0.3 ng/mL. The sponsor is using the LoQ, 0.3 ng/mL, as the lowest limit of the measuring range.

e. *Analytical specificity:*

Cross-reactivity and endogenous interference studies:

Analytical specificity was evaluated on the Elecsys 2010 with the Elecsys Troponin I STAT reagent for possible cross reactants of skeletal muscle TnI, recombinant cardiac troponin T (TnT), purified troponin C (TnC) and skeletal muscle TnT, as well as endogenous interferents of hemolysis, biotin, lipemia, bilirubin and rheumatoid factors.

Two samples of different Troponin I concentrations were analyzed in duplicate for each cross reactant and interferent. One sample had Troponin I values within the clinical decision range of 0.3-0.5 ng/mL. The second sample had Troponin I values ranging from approximately 2.5-2.8 ng/mL.

Samples were split and spiked with the appropriate compounds at various concentrations and compared to an unaltered aliquot of the sample.

Concentrations up to 2000 ng/mL of skeletal TnI, recombinant cardiac TnT, purified troponin C (TnC), and skeletal muscle TnT did not cross-react with the assay.

Hemoglobin up to 0.4 g/dL, biotin up to 30 ng/mL, lipemia (Intralipid) up to 1,500 mg/dL, bilirubin up to 25 mg/dL and rheumatoid factors up to 1,500 IU/mL did not interfere with the assay. Labeling states that grossly hemolyzed samples should not be used.

52 potentially interfering common compounds and prescription drugs were tested in 100 times higher than expected dose level in plasma. A list of these compounds can be found in the package insert.

f. Assay cut-off:

The sponsor determined the AMI cut-off to be 0.3 ng/mL. See clinical sensitivity 3a below.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison was conducted between the predicate and the Elecsys 2010 using the Troponin I STAT reagent. 114 samples with troponin I values covering the measuring range were analyzed in singlicate. Regression was calculated using Passing-Bablock, Standardized Linearity and Deming equations. The results are summarized below.

Troponin I STAT/Elecsys 2010 vs Predicate

	Slope (95% CI)	Intercept (95% CI)	Correlation
Passing-Bablock	0.7954 (0.7586, 0.8553)	0.2187 (0.1565, 0.2787)	Tau =.8058
Linear Regression	0.7878 (0.7403,0.8353)	0.3204 (0.1668, 0.4740)	r = 0.9465
Deming Regression	0.8198 (0.7726, 0.8673)	0.2168 (0.632, 0.3704)	r = 0.9519

Based on the method comparison, clinical data was used to determine substantial equivalency. See section M.3.a. To demonstrate equivalence between the two reagent systems, comparisons were performed between the Troponin I immunoassay reagent on the MODULAR Analytics E170 and the Troponin I STAT immunoassay reagent on the Elecsys 2010. 115 samples were analyzed on the E170 and the Elecsys 2010. All samples were run in

singlicate and covered the measuring range. Regression was calculated using Passing-Bablock, Standardized Linearity and Deming equations. The results are summarized below.

Troponin I/E170 vs Troponin I Stat/Elecsys 2010

	Slope (95% CI)	Intercept (95% CI)	Correlation
Passing-Bablock	0.9743 (0.9637, 0.9896)	-0.0172 (-0.0713, 0.0174)	Tau =0.9616
Linear Regression	0.9934 (0.9720, 1.0148)	-0.0623 (-0.2099, 0.0854)	r = 0.9971
Deming Regression	1.0000 (0.9786, 1.0214)	-0.1080 (-0.2556, 0.0397)	r = 0.9934

b. Matrix comparison:

In order to demonstrate equivalence of TnI results among serum, lithium heparin, K2-EDTA and K3-EDTA plasmas, sample pairs were evaluated across the measuring range (0.33-24.83 ng/mL). Both native and spiked samples were included in the studies. Results of the plasmas versus serum were analyzed by Passing-Bablock, Linear Regression and Deming Regression. Results are summarized below:

Serum vs. K_2-EDTA		**Passing/Bablok**	**LinReg**	**Deming**	**Method**	**Correlation**
Slope	N=39	0.9696	0.9425	0.9489	Kendall's tau	0.9487
	LCL 95%	0.9530	0.9048	0.9112	Spearman's rho	0.9903
	UCL 95%	0.9870	0.9802	0.9866	Pearson's r	0.9929
Intercept		0.0171	0.1771	0.1095		
	LCL 95%	-0.0795	-0.2206	-0.2883		
	UCL 95%	0.1716	0.5749	0.5072		

Serum vs. K_3-EDTA		**Passing/Bablok**	**LinReg**	**Deming**	**Method**	**Correlation**
Slope	N=21	0.9660	0.9407	0.9468	Kendall's tau	0.9143
	LCL 95%	0.9362	0.8876	0.8937	Spearman's rho	0.974
	UCL 95%	0.9939	0.9938	0.9999	Pearson's r	0.9932
Intercept		-0.0166	0.2492	0.1757		
	LCL 95%	-0.2011	-0.3883	-0.4618		
	UCL 95%	0.3917	0.8867	0.8132		

Serum vs. Lithium Heparin		Passing/Bablok	LinReg	Deming	Method	Correlation
Slope	N= 49	1.0000	0.9423	0.9702	Kendall's tau	0.8844
	LCL 95%	0.9191	0.8734	0.9013	Spearman's rho	0.975
	UCL 95%	1.0372	1.0112	1.0391	Pearson's r	0.9703
Intercept		-0.0765	0.1271	-0.1025		
	LCL 95%	-0.1257	-0.4391	-0.6687		
	UCL 95%	0.1097	0.6933	0.4637		

3. Clinical studies:

a. Clinical Sensitivity:

A prospective study was conducted with 402 patients at 5 sites (2 US, 3 non-US). Inclusion criteria were chest pain for 24 hours and clinicians' diagnoses using the ESC/AHA/ACC criteria on the Elecsys 2010 and Modular Analytics E170. A breakdown of AMI and non-AMI frequency by site is below.

	Site 1	Site 2	Site 3	Site 4	Site 5	Total
Non-AMI	123	99	11	4	74	311 (77%)
AMI	25	48	1	5	12	91 (23%)
Total	148	147	12	9	86	402

Sensitivity and specificity of the Acute Myocardial Infarction (AMI) cutoff as defined by ESC/ACC /AHA criteria for the candidate device were evaluated at various time intervals against the predicate. Blood samples were taken at 0-6 hrs, 6-12 hrs, and > 12 hrs. post admission. The summarized sensitivities and specificities are below:

Time	Sensitivity % (n/N)	LCL Sens %	UCL Sens %
All	90.11(82/91)	82.26	94.71
0-6h	80.90(71/97)	72.19	88.35
6-12h	84.62(44/52)	72.19	88.35
> 12h	90.70(39/43)	78.40	96.32

Time	Specificity % (n/N)	LCL Spec %	UCL Spec %
All	97.75(304/311)	95.43	98.91
0-6h	98.06(304/310)	95.84	99.11
6-12h	99.00(199/201)	95.84	99.11
> 12h	95.52(65/68)	87.81	98.49

b. Clinical specificity:

See 3.a. clinical sensitivity above.

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

4. Clinical cut-off:

A separate cutoff study was performed prior to the clinical studies performed in M.3.a above. 652 subjects from one US site and one non-US site were evaluated for chest pain. Using the clinician's diagnosis, based on the ESC/AHA/ACC criteria, 358 subjects (102 females, 256 males) were included in the determination of the AMI cut-off study. Multiple blood samples were drawn and analyzed using the Troponin I assay and plotted using ROC analysis. A summary is below showing the standard deviation, and lower and upper confidence limits.

The cut-off was determined to be 0.3 ng/mL with a CV ≤ 10%.

AUC	Std	LCL	UCL
0.9565	0.0158	0.91263	0.97885

5. Expected values/Reference range:

In a study of 1,137 apparently healthy individuals from 4 US sites and 2 European sites, the troponin I levels were determined to be < 0.3 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.