May 17, 2019

Siemens Healthcare Diagnostics, Inc.
Laura Duggan
Sr. Mgr. Regulatory Affairs
500 GBC Drive
Newark, DE 19714

Re: K190675
Trade/Device Name: Dimension EXL High-Sensitivity Troponin I (TNIH) Assay
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine phosphokinase/creatine kinase or isoenzymes test system
Regulatory Class: Class II
Product Code: MMI
Dated: March 18, 2019
Received: March 19, 2019

Dear Laura Duggan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for Kellie B. Kelm, Ph.D.
Acting Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure:

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k190675

Device Name
Dimension EXL High-Sensitivity Troponin I (TNIH) assay

Indications for Use *(Describe)*
The Dimension EXL High-Sensitivity Troponin I (TNIH) assay is for in vitro diagnostic use in the quantitative measurement of cardiac troponin I in human plasma using the Dimension EXL integrated chemistry system with LOCI module. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SECTION 7: 510(K) SUMMARY

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

ASSIGNED 510(K) NUMBER

The assigned 510(k) number is ___k190675_____.

APPLICANT AND DATE

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March 14, 2019

MANUFACTURER

Siemens Healthcare Diagnostics Inc.
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Registration Number: 2517506

REGULATORY INFORMATION

Regulatory Submission for the Dimension EXL High-Sensitivity Troponin I (TNIH) Assay

Device:	Immunoassay method, troponin subunit
Regulation Description:	Creatine phosphokinase/creatine kinase or isoenzymes test system
Proprietary Name:	Dimension EXL High-Sensitivity Troponin I (TNIH) Assay
Regulation Number:	21CFR862.1215
Classification:	Class II
Product Code:	MMI

Panel:	Clinical Chemistry
Predicate Device:	Elecsys Troponin T Gen 5 STAT (K162895)

DEVICE DESCRIPTION

DIMENSION EXL HIGH-SENSITIVITY TROPONIN I (TNIH) ASSAY

The Dimension EXL TNIH assay is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI® technology. The LOCI reagents include two synthetic bead reagents and two biotinylated anti-cardiac troponin I monoclonal antibody fragments. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a third anti-cardiac troponin I monoclonal antibody and contains chemiluminescent dye. Sample is incubated with Chemibeads and biotinylated antibodies to form bead-cardiac troponin I-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the cardiac troponin I concentration in the sample

Lithium heparin plasma specimens may be used. The reagent is stored unopened at 2 – 8 °C, is stable sealed on system for 30 days and opened on the system for 7 days. Calibration is performed every 21 days for a reagent lot.

INTENDED USE/INDICATIONS FOR USE

DIMENSION EXL HIGH-SENSITIVITY TROPONIN I (TNIH) ASSAY

The Dimension EXL High-Sensitivity Troponin I (TNIH) assay is for in vitro diagnostic use in the quantitative measurement of cardiac troponin I in human plasma using the Dimension EXL integrated chemistry system with LOCI module. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

SUBSTANTIAL EQUIVALENCE COMPARISON

Below is a substantial equivalence comparison for the Dimension EXL High-Sensitivity Troponin I (TNIH) Assay vs. the Elecsys Troponin T Gen 5 STAT (K162895) device.

Feature	**Predicate Device:** Elecsys Troponin T Gen 5 STAT (K162895)	**New Device:** DIMENSION EXL HIGH-SENSITIVITY TROPONIN I (TNIH) ASSAY
Intended Use :	Immunoassay for the in vitro quantitative determination of cardiac troponin T (cTnT) in lithium heparin plasma.	The Dimension EXL High-Sensitivity Troponin I (TNIH) assay is for in vitro diagnostic use in the quantitative measurement of cardiac troponin I in human plasma using the Dimension EXL integrated chemistry system with LOCI module.
Indications for Use:	The immunoassay is intended to aid in the diagnosis of myocardial infarction.	The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).
Device Technology:	Electrochemiluminescence immunoassay	Homogeneous immunoassay
Sample Type:	Lithium Heparin Plasma	Lithium Heparin plasma
Expected Values:	99th percentile were determined to be: ▪ 19 ng/L for both ▪ 14 ng/L for females ▪ 22 ng/L for males	99th percentile determined for for plasma 60.4 pg/mL overall female 51.4 pg/mL plasma male 76.2 pg/mL plasma
Calibration Frequency:	after 12 weeks when using the same reagent lot	21 days for any one lot
Analytical Measuring Interval:	6-10,000 ng/L	4.0 – 25,000.0 pg/mL [ng/L]
Interferences:	No interference in plasma at: Hemoglobin – 100 mg/dL Bilirubin 25 mg/dL Lipemia (Intralipid®) – 1500 mg/dL	No interferences in plasma at approximately 40 pg/mL and approximately 1350 pg/mL of cardiac troponin I from: Hemoglobin – 400 mg/dL

		Bilirubin (Unconjugated) – 40 mg/dL Bilirubin (Conjugated) – 30 md/dL Lipemia (Intralipid®) – 3000 mg/dL
Calibrators:	Elecsys Troponin T Gen 5 STAT calibrators (CalSet Troponin T Gen 5 STAT)	LOCI TNIH Calibrator, Cat. No. RC627

SUMMARY OF PERFORMANCE TESTING

Assay performance results for the Dimension EXL High-Sensitivity Troponin I (TNIH) assay was determined by processing the appropriate body fluids. Summary statistics for each are provided. The following data represent typical assay performance. All data were collected on the Dimension EXL with LM System.

DETECTION LIMIT

The Limit of Blank (LoB) and Limit of Detection (LoD) were evaluated in accordance with CLSI EP17-A2 Protocols for Determination of Limits of Detection and Limits of Quantitation: Approved Guideline.

Assessment of LoB was the 95th percentile of all values (sorted from lowest to highest), using non-parametric approach. LoB Rank Position = 0.5 +0.95*B, where B=total reps=60; Rank = 57.5

The nonparametric approach described in EP17-A2 was followed to determine the Limit of Detection. LoD was tested separately for lithium heparin specimens.

Dimension EXL High-Sensitivity Troponin I (TNIH) - Limit of Detection Results		
Limit	Protocol	Result
LoB	5 samples with no analyte (calibrator Level A, BSA based with HEPES buffer 5 individual vials) were tested (N=4) for 3 days, one run per day, 3 reagent lots	1.0 pg/mL
LoD	At least 5 low analyte samples were tested (N=4) for 3 days for native lithium heparin plasma, one run per day, 3 reagent lots	1.0 - 1.8 pg/mL

Results are consistent with the claim of 2.7 pg/mL for LoD and 1.1 pg/mL for LoB.

LOQ

The Limit of Quantitation (LoQ) for plasma was determined as the analyte level with a within-lab CV of less than or equal to 20.0%. Testing was completed two times a day (n=2) for at least 20 days for a total of 80 replicates with at least 6 native lithium heparin plasma pools on one instrument.

LoQ Lot Summary

Reagent Lot	Lot-1	Lot-2	Lot-3
Lithium Heparin Plasma 20% CV (pg/mL)	1.1	2.1	2.3

The LoQ for TNIH of 4.0 pg/mL is consistent with the data.

10% CV LIMIT

For lithium heparin plasma the analyte level with a within-lab CV of less than or equal to 10.0% was determined using CLSI EP5-A3, Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Third Edition. Testing was completed two times a day (n=2) for at least 20 days for a total of 80 replicates with at least 6 native lithium heparin plasma pools on one instrument.

10% CV Lot Summary

Reagent Lot	Lot-1	Lot-2	Lot-3
Lithium Heparin Plasma 10% CV (pg/mL)	3.2	5.3	5.8

The 10% CV limit for Dimension EXL TNIH of 12.0 pg/mL is consistent with the data.

PRECISION STUDIES

Precision testing was performed in accordance with CLSI EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Third Edition. Precision was tested n = 2 replicates, two times a day for at least 20 days for a total of 80 replicates with controls and plasma pools on one instrument. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP05-A3. The data are summarized in the following table. All precision goals were met.

		Repeatability		Within-Lab	
Material	**Mean pg/mL [ng/L]**	**SD[a] pg/mL [ng/L]**	**%CV[b]**	**SD pg/mL [ng/L]**	**%CV**
Plasma 1	48.0	1.11	2.3	2.87	6.0
Plasma 2	71.8	1.45	2.0	2.09	2.9
Plasma 3	155.7	2.75	1.8	4.62	3.0
QC	7411.7	145.59	2.0	246.56	3.3

[a]SD = standard deviation

[b] CV = coefficient of variation

LINEARITY STUDY

Linearity was evaluated with 16 lithium heparin plasma samples which spanned the assay measuring interval. Each was prepared by mixing high and low concentration samples across the measurement interval as described in CLSI Evaluation of the Linearity of Quantitative Measurement Procedure (EP06-A). The high samples and the low samples for lithium heparin plasma were native. At least five replicates were measured for each sample. The mean of these replicates was used for the calculations.

The assay was considered linear across the measuring interval if the p values of nonlinear terms in the quadratic and cubic fit equations are nonsignificant ($p \leq 0.05$). If the p-value is > 0.05, then the allowable bias is ≤ 10% or 4 pg/mL, whichever is greater.

The testing confirmed linearity from 4.0 – 25,000.0 pg/mL.

INTERFERENCES

CLSI EP7-A2 was followed for the interference testing. The interference study was conducted using a “paired difference scenario” approach where these compounds were spiked into fresh sample pools containing either low or high levels of troponin in lithium heparin troponin I pools. All exogeneous compounds were spiked into the troponin control pools at two levels. Endogeneous compounds were only tested at elevated levels as they are natively found in specimen samples.

Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference. Dilution studies were conducted to determine the level at which the spiked substance no longer displayed significant interference. Dilution studies were conducted at two analyte concentrations, if both sample pools show significant interference.

No interference was detected at the following analyte concentrations.

Substance Tested	**Substance concentration**	**Bias (%)**
Hemoglobin hemolysate (monomer)	400 mg/dL [0.25 mmol/L]	<10
Bilirubin (conjugated)	30 mg/dL [356 µmol/L]	<10
Bilirubin (unconjugated)	40 mg/dL [684 µmol/L]	<10
Lipemia (Intralipid®)	3000 mg/dL [33.9 mmol/L]	<10

	Low or Therapeutic Concentration		**High or Toxic Concentration**	
Potential Interferent	**Conventional Units**	**SI Units**	**Conventional Units**	**SI Units**
Abciximab	0.4 mg/dL	NA	4.0 mg/dL	NA

Acetaminophen	2.0 mg/dL	133 µmol/L	20.0 mg/dL	1324 µmol/L
Acetylsalicylic acid	26.1 mg/dL	1.45 mmol/L	65.2 mg/dL	3.62 mmol/L
Allopurinol	1.3 mg/dL	91.9 µmol/L	4.0 mg/dL	294 µmol/L
Amiodarone	0.2 mg/dL	2.6 µmol/L	0.6 mg/dL	8.92 µmol/L
Ampicillin	1.1 mg/dL	29.1 µmol/L	5.6 mg/dL	152 µmol/L
Ascorbic acid	1.2 mg/dL	68.5 µmol/L	6.0 mg/dL	342 µmol/L
Atenolol	0.1 mg/dL	4.1 µmol/L	1.0 mg/dL	37.6 µmol/L
Biotin	10 ng/mL	0.04 µmol/L	300 ng/mL	1.2 µmol/L
Caffeine	1.3 mg/dL	64.4 µmol/L	6.0 mg/dL	308 µmol/L
Captopril	0.1 mg/dL	4.6 µmol/L	0.5 mg/dL	23 µmol/L
Cefoxitin	12.63 mg/dL	281 µmol/L	69.5 mg/dL	1546 µmol/L
Cholesterol	NA**	NA	300 mg/dL	7.8 mmol/L
Cinnarizine	0.0285 mg/dL	0.8 µmol/L	2.5 mg/dL	67.8 µmol/L
Clopidogrel	0.32 mg/dL	9.9 µmol/L	7.5 mg/dL	233 µmol/L
Cocaine	0.05 mg/dL	1.6 µmol/L	1.0 mg/dL	33 µmol/L
Dextran 40	15 g/L	375 µmol/L	45 g/L	1125 µmol/L
Digitoxin	17 ng/mL	22.2 nmol/L	60 ng/mL	78.4 nmol/L
Digoxin	1.4 ng/mL	1.8 nmol/L	6.1 ng/mL	7.8 nmol/L
Diltiazem	0.025 mg/dL	0.55 µmol/L	0.68 mg/dL	15 µmol/L
Disopyramide	0.45 mg/dL	10.4 µmol/L	1.3 mg/dL	29.5 µmol/L
Dopamine	0.04 mg/dL	1.96 µmol/L	0.11 mg/dL	5.87 µmol/L
Doxycycline	1.1 mg/dL	22.5 µmol/L	3.2 mg/dL	67.5 µmol/L
Erythromycin	1.1 mg/dL	15 µmol/L	6.0 mg/dL	81.6 µmol/L
Furosemide	2.0 mg/dL	60.4 µmol/L	6.0 mg/dL	181 µmol/L
Ibuprofen	4.0 mg/dL	194.3 µmol/L	50 mg/dL	2425 µmol/L
Isosorbide dinitrate	50.1 ng/mL	212 nmol/L	150.2 ng/mL	636 nmol/L
Lisinopril	0.01 mg/dL	0.25 µmol/L	0.33 mg/dL	0.74 µmol/L
Low MW Heparin	0.85 U/mL	NA	2.0 U/mL	NA
Lovastatin	17.2 ng/mL	42.4 nmol/L	80 ng/mL	197.8 nmol/L
Methotrexate	50 mg/dL	1.1 mmol/L	91 mg/dL	2 mmol/L
Methyldopa	0.48 mg/dL	20.1 µmol/L	1.69 mg/dL	70.9 µmol/L
Methylprednisolone	1.65 mg/dL	44 µmol/L	4.0 mg/dL	106.8 µmol/L
Mexiletine	0.15 mg/dL	7 µmol/L	0.48 mg/dL	22.3 µmol/L
Nicotine	0.004 mg/dL	0.2 µmol/L	0.10 mg/dL	6.2 µmol/L
Nifedipine	0.013 mg/dL	361.3 nmol/L	0.04 mg/dL	1156.1 nmol/L
Nitrofurantoin	0.20 mg/dL	8.4 µmol/L	0.40 mg/dL	16.8 µmol/L
Nitroglycerine	7.5 ng/mL	33 nmol/L	160 ng/mL	704.5 nmol/L
Phenobarbital	2.5 mg/dL	107.8 µmol/L	10.0 mg/dL	431.5 µmol/L
Phenytoin	1.36 mg/dL	49.6 µmol/L	5.43 mg/dL	198 µmol/L
Primidone	1.1 mg/dL	48.2 µmol/L	4.0 mg/dL	183.5 µmol/L
Propranolol	0.06 mg/dL	1.93 µmol/L	0.23 mg/dL	7.71 µmol/L
Protein, Albumin	NA**	NA	6 g/dL	60 g/L
Protein, Gamma Globulin	2.5 g/dL	NA	NA	NA
Protein, Total	NA**	NA	12 g/dL	NA
Quinidine	0.38 mg/dL	11.7 µmol/L	1.2 mg/dL	37 µmol/L
Rheumatoid Factor	750 IU/mL	NA	1500 IU/mL	NA
Simvastatin	0.004 ug/mL	0.01 µmol/L	32 ug/mL	76.5 µmol/L

Theophylline	1.25 mg/dL	69.4 µmol/L	4.0 mg/dL	222.2 µmol/L
Tissue plasminogen activator (TPA)	0.52 µg/mL	NA	2.3 µg/mL	NA
Thyroxine	0.23 mg/dL	0.3 µmol/L	0.6 mg/dL	0.8 µmol/L
Triglyceride	500 mg/dL	NA	1000 mg/dL	NA
Trimethoprim	1.25 mg/dL	43.1 µmol/L	4.0 mg/dL	138.3 µmol/L
Verapamil	0.035 mg/dL	0.8 µmol/L	0.22 mg/dL	4.4 µmol/L
Warfarin	0.20 mg/dL	6.6 µmol/L	1.0 mg/dL	32.5 µmol/L

**Testing at low concentrations was not appropriate for these endogenous substances.

ANALYTICAL SPECIFICITY

Cross-reactivity was determined following the governing standard CLSI document EP07-A2: *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition.* Cross-reactivity was tested at cTnI concentration of range of 20-60 pg/mL in native lithium heparin pools as well as in the absence of cTnI**.** The cross-reactants were tested at a single concentration near the upper limit of its therapeutic range. TNIH assay results from the spiked samples were compared with those of unspiked control samples. Percent cross-reactivity is calculated as:

$$\% \text{ Cross-reactivity} = \frac{[\text{measured analyte}] - [\text{control analyte}] \times 100}{[\text{cross-reactant}]}$$

Cross-reactant	Amount ng/mL [µg/L]	Cross-reactivity (%)
Cardiac Troponin T	1000	0.003
Skeletal Troponin I	1000	0.001
Tropomyosin	1000	ND
Actin	1000	ND
Troponin C	1000	ND
Myosin Light Chain	1000	ND
Myoglobin	1000	ND
CK-MB	1000	ND

*ND= Not detectable

HIGH DOSE HOOK EFFECT

The high dose hook effect of the TNIH assay was assessed. Normal human lithium heparin plasma were spiked with calibrator antigen. A dilution series was created and tested. No hook effect was found at 1,000,000 pg/mL troponin on the Dimension EXL TNIH assay.

DILUTION RECOVERY

Dilution recovery was evaluated for plasma at 1:2 and 1:5 dilutions using CTNI SDIL as diluent. Native human plasma samples were pooled to obtain at least three unique patient samples with TNIH levels ≥75% of the measuring interval and at least two samples above the measuring interval. For samples above the assay measuring interval the expected or neat value was determined using a 1:2 dilution in normal human plasma. Testing supported use of the diluent for over-range samples.

CALIBRATION STABILITY

The calibration stability for the TNIH assay on the Dimension EXL was determined by reading the recovery of the calibrators, commercial QC, a low patient pool and a high pool over time. The p-value of the regression slope was determined. Passing results were a p-value greater than or equal to 0.05 or drift less than or equal to the LoQ or less than or equal to10% for values up to 20,000 pg/mL and less than or equal to 13% for values greater than 20,000 pg/mL. Calibration interval was measured to be 21 days.

OPEN WELL STABILITY

The open well stability for the TNIH assay on the Dimension EXL was determined by reading the recovery of the calibrators and a low patient pool. On the first day of the study reagent packs were opened on the system and analyte was measured over the desired time interval. The p-value of the regression slope was determined. Passing results were a p-value greater than or equal to 0.05 or drift less than or equal to the LoQ or less than or equal to10% for values up to 20,000 pg/mL and less than or equal to 13% for values greater than 20,000 pg/mL. The stability of the reagents opened onboard the instrument was 7 days per well set.

SAMPLE STABILITY

Separated samples are stable for 8 hours at room temperature and for 24 hours when stored at 2-8 °C. Samples can be frozen at or below -20 °C for up to 40 days in a non-frost free freezer and at or below -70 °C for up to 1 year. A linear regression analysis of the observed Troponin % Bias value (Y-axis) versus time (X-axis) was completed for each matrix. The acceptance criteria were the lower bound of the one-sided 95% confidence interval of the regression line is ≤-10% and all individual data points had a bias of ≤ -20% when compared to time zero.

EXPECTED VALUES

Lithium heparin plasma specimens were collected from apparently healthy individuals from the United States who ranged in age from 22–91 years of age. Each specimen

was frozen, thawed and assayed once. The 99th percentile values were determined using the non-parametric statistical method described in CLSI Guidance EP28-A3c. Sample type, gender, and age had no statistically significant effect on the 99th percentile.

The combined gender and the more commonly used sample type of lithium heparin were used to determine the overall observed 99th percentile of 60.4 pg/mL [ng/L]. Two female subjects had troponin values of approximately 400 pg/mL and 4700 pg/mL, and were considered to be outliers. These results were not included in the 99th percentile-determination.

The 99th percentile values determined for lithium heparin plasma (female, male, and combined) are shown in the following table. The 90% confidence intervals demonstrate that there is no statistical basis for using separate 99th percentile values based on gender or sample type.

Sample Type	**Gender**	**n**	**99th Percentile[a] pg/mL [ng/L]**	**90% CI[b] pg/mL [ng/L]**
Lithium Heparin	Female	1017	51.4	35.6 to 109.2
	Male	1003	76.2	42.3 to 117.0
	Combined	2020	60.4	43.2 to 81.3

[b] confidence interval

CLINICAL PERFORMANCE

A prospective study was performed to assess diagnostic accuracy for approximately 2500 subjects in lithium heparin plasma sample types to evaluate clinical performance. Specimens were collected at 29 emergency departments across the United States, from subjects presenting with symptoms consistent with acute coronary syndrome (ACS).

All subject diagnoses were adjudicated by panels of certified cardiologists and emergency physicians according to the Third Universal Definition Of Myocardial Infarction - consensus guideline endorsed by the European Society of Cardiology (ESC), the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), and the World Heart Federation (WHF). The observed AMI prevalence in this study was 13.0 %.

The clinical concordance study evaluated clinical sensitivity, clinical specificity, positive predictive value (PPV) and negative predictive value (NPV) of the Dimension EXL TNIH assay in terms of its correlation to the the diagnosis of AMI. The results were analyzed using the serial sampling time points collected during the emergency department visit. A positive is defined as a sample exceeding the 99th percentile cutoff at the particular time point. The results are presented using serial timed intervals analyzed according to the time of presentation to the emergency department. The pooled gender results based

on time of presentation to the emergency department, calculated using the overall 99th percentile of 60.4 pg/mL, are summarized in Table 1.

Table1: Pooled gender results based on time from presentation to the emergency department

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time since presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0 – < 1.5	138	78.3	70.7-84.3	978	92.9	91.2-94.4	177	61.0	53.7-67.9	939	96.8	95.5-97.8
≥ 1.5 – < 2.5	240	88.8	84.1-92.2	1658	91.6	90.1-92.8	353	60.3	55.2-65.3	1545	98.3	97.5-98.8
≥ 2.5 – < 3.5	199	89.9	85.0-93.4	1379	90.6	89.0-92.1	308	58.1	52.5-63.5	1270	98.4	97.6-99.0
≥ 3.5 – < 4.5	144	92.4	86.8-95.7	1094	91.2	89.4-92.8	229	58.1	51.6-64.3	1009	98.9	98.1-99.4
≥ 4.5 – < 6	67	95.5	87.6-98.5	463	89.2	86.0-91.7	114	56.1	47.0-64.9	416	99.3	97.9-99.8
≥ 6 – < 9	191	92.7	88.1-95.6	917	88.0	85.7-90.0	287	61.7	55.9-67.1	821	98.3	97.2-99.0
≥ 9 – < 24	215	93.0	88.8-95.7	849	86.2	83.7-88.4	317	63.1	57.7-68.2	747	98.0	96.7-98.8
≥ 24	63	95.2	86.9-98.4	256	86.3	81.6-90.0	95	63.2	53.1-72.2	224	98.7	96.1-99.5

Results for females based on time of presentation to the emergency department, calculated using the female-specific 99th percentile of 51.4 pg/mL for plasma are summarized in Table 2.

Table 2: Results for females based on time from presentation to the emergency department

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time since presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0 – < 1.5	42	83.3	69.4-91.7	407	94.6	92.0-96.4	57	61.4	48.4-72.9	392	98.2	96.4-99.1
≥ 1.5 – < 2.5	78	91.0	82.6-95.6	728	91.9	89.7-93.7	130	54.6	46.0-62.9	676	99.0	97.9-99.5
≥ 2.5 – < 3.5	73	94.5	86.7-97.8	624	92.0	89.6-93.9	119	58.0	49.0-66.5	578	99.3	98.2-99.7
≥ 3.5 – < 4.5	51	94.1	84.1-98.0	492	90.9	88.0-93.1	93	51.6	41.6-61.5	450	99.3	98.1-99.8
≥ 4.5 – < 6	25	96.0	80.5-99.3	242	85.5	80.6-89.4	59	40.7	29.1-53.4	208	99.5	97.3-99.9
≥ 6 – < 9	68	94.1	85.8-97.7	380	87.9	84.2-90.8	110	58.2	48.8-67.0	338	98.8	97.0-99.5
≥ 9 – < 24	72	93.1	84.8-97.0	348	88.5	84.7-91.4	107	62.6	53.2-71.2	313	98.4	96.3-99.3
≥ 24	26	100.0	87.1-100.0	111	82.0	73.8-88.0	46	56.5	42.2-69.8	91	100.0	95.9-100.0

Results for males based on time of presentation to the emergency department, calculated using the male-specific 99th percentile of 76.2 pg/mL for plasma are summarized in Table 3.

Table 3: Results for males based on time from presentation to the emergency department

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time since presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0 – < 1.5	96	74.0	64.4-81.7	571	92.3	89.8-94.2	115	61.7	52.6-70.1	552	95.5	93.4-96.9
≥ 1.5 – < 2.5	162	85.2	78.9-89.8	930	92.5	90.6-94.0	208	66.3	59.7-72.4	884	97.3	96.0-98.2
≥ 2.5 – < 3.5	126	84.9	77.6-90.1	755	91.0	88.7-92.8	175	61.1	53.8-68.1	706	97.3	95.8-98.3
≥ 3.5 – < 4.5	93	86.0	77.5-91.6	602	92.7	90.3-94.5	124	64.5	55.8-72.4	571	97.7	96.1-98.7
≥ 4.5 – < 6	42	88.1	75.0-94.8	221	91.4	87.0-94.4	56	66.1	53.0-77.1	207	97.6	94.5-99.0
≥ 6 – < 9	123	88.6	81.8-93.1	537	90.9	88.1-93.0	158	69.0	61.4-75.7	502	97.2	95.4-98.3
≥ 9 – < 24	143	90.9	85.1-94.6	501	87.2	84.0-89.9	194	67.0	60.1-73.2	450	97.1	95.1-98.3
≥ 24	37	89.2	75.3-95.7	145	91.0	85.3-94.7	46	71.7	57.5-82.7	136	97.1	92.7-98.9

CONCLUSION

The Dimension EXL High-Sensitivity Troponin I (TNIH) Assay is substantially equivalent to the Elecsys Troponin T Gen 5 STAT (K162895) in principle and performance based on the similarity of device designs and function demonstrated through performance attributes presented.