July 25, 2024

Siemens Healthcare Diagnostics Inc.
Amy Tyler
Regulatory Affairs Professional
500 GBC Drive, P.O. Box 6101
Mail Stop 514
Newark, Delaware 19714

Re: K241165
Trade/Device Name: Atellica® IM High-Sensitivity Troponin I (TnIH)
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine Phosphokinase/Creatine Kinase Or Isoenzymes Test System
Regulatory Class: Class II
Product Code: MMI
Dated: April 22, 2024
Received: April 26, 2024

Dear Amy Tyler:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Deputy Division Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K241165

Device Name
Atellica® IM High-Sensitivity Troponin I (TnIH)

Indications for Use *(Describe)*
The Atellica® IM High-Sensitivity Troponin I (TnIH) assay is for in vitro diagnostic use in the quantitative measurement of cardiac troponin I in human serum or plasma (lithium heparin) using the Atellica® IM Analyzer. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

The Atellica IM TnIH assay can be used as an aid in prognosis for 30-, 90-, 182-, and 365-day all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS). MACE consists of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization.

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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510(k) Summary of Safety and Effectiveness

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Act of 1990.

The assigned 510(k) number is: K241165

1. Date Prepared

July 25, 2024

2. Applicant Information

Contact: Amy Tyler
Regulatory Affairs Professional
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Newark, DE 19714, USA
Phone: 610-836-1390
Email: amy.c.tyler@siemens-healthineers.com

3. Regulatory Information

Trade Name	Atellica® IM High-Sensitivity Troponin I (TnIH)
Model Numbers	10997840 (1-pack); 10997841 (5-pack)
Device Classification Name	Immunoassay Method, Troponin Subunit
Regulation Number	21 CFR 862.1215
Regulation Description	Creatine phosphokinase/creatine kinase or isoenzymes test system
Product Code	MMI
FDA Classification	Class II
Review Panel	Clinical Chemistry

4. Predicate Device Information

Device Name: VITROS Troponin I ES Assay

510(k) Number: K062838

5. Intended Use / Indications for Use

The Atellica® IM High-Sensitivity Troponin I (TnIH) assay is for *in vitro* diagnostic use in the quantitative measurement of cardiac troponin I in human serum or plasma (lithium heparin) using the Atellica® IM Analyzer. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

The Atellica IM TnIH assay can be used as an aid in prognosis for 30-, 90-, 182-, and 365-day all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS). MACE consists of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization.

6. Device Description

The Atellica® IM TnIH assay is a 3-site sandwich immunoassay using direct chemiluminescent technology. The Solid Phase reagent consists of magnetic particles conjugated with streptavidin with 2 bound biotinylated capture monoclonal antibodies, each recognizing a unique cTnI epitope.

The Lite Reagent comprises a conjugate with an architecture consisting of a proprietary acridinium ester and a recombinant anti-human cTnI sheep Fab covalently attached to bovine serum albumin (BSA) for chemiluminescent detection.

A direct relationship exists between the amount of cTnI present in the patient sample and the amount of relative light units (RLUs) detected by the system.

The Atellica® IM TnIH assay consists of the components described in the following table.

Component	Volume	Ingredients
Atellica® IM TnIH ReadyPack® primary reagent pack (included in assay kit)		
Lite Reagent	8.0 mL/reagent pack	Bovine serum albumin (BSA) conjugated to a recombinant monoclonal (sheep) Fab anti-human cTnI (~0.2-0.4 µg/mL) labeled with acridinium ester in HEPES buffer; stabilizers; preservatives
Solid Phase	13.0 mL/reagent pack	Streptavidin-coated magnetic particles (0.45 mg/mL) with 2 biotinylated (mouse and sheep) monoclonal anti-troponin I antibodies in buffer; stabilizers; preservatives
Atellica® IM TnIH Calibrator (included in assay kit)		
Atellica® IM TnIH CAL L	1.0 mL/vial	HEPES buffer; bovine serum albumin (BSA); surfactants; preservatives
Atellica® IM TnIH CAL H	1.0 mL/vial (lyophilized)	After reconstitution, human serum; human cTnI; preservatives
Atellica® IM TnIH Master Curve Material (sold separately)*		
Atellica® IM TnIH MCM (master curve material), 1-5	1.0 mL/vial (lyophilized)	Human troponin I complex in a human serum base, with preservatives

*Additional information for this product is not included in this 510(k) because as of 2017-04-13, this device (Product Code JJX; Regulation No. 862.1660; Single (Specified) Analyte Controls (Assayed and Unassayed)) is exempt from pre-market notification requirements, as described in FDA Notice Docket No. FDA-2017-N-1610.

7. Purpose of the Submission

The purpose of this 510(k) premarket notification is to add an indication for use so that the assay can be used as an aid in prognosis for 30-, 90-, 182-, and 365-day all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS). MACE consists of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization.

8. Comparison of Candidate Device and Predicate Devices

The following table describes the similarities and differences between the Atellica® IM High-Sensitivity Troponin I (TnIH) assay (Candidate Device) and the VITROS Troponin I ES Assay (Predicate Device).

Comparison Table of Candidate Device and Predicate Device

Attributes	Candidate Device Atellica® IM High-Sensitivity Troponin I (TnIH)	Predicate Device VITROS Troponin I ES Assay – K062838
Intended Use	The Atellica® IM High-Sensitivity Troponin I (TnIH) assay is for *in vitro* diagnostic use in the quantitative measurement of cardiac troponin I in human serum or plasma (lithium heparin) using the Atellica® IM Analyzer. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI). The Atellica® IM TnIH assay can be used as an aid in prognosis for 30-, 90-, 182-, and 365-day all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS). MACE consists of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization.	For the quantitative measurement of cardiac Troponin I (cTnI) in human serum and plasma (heparin and EDTA) using the VITROS ECi/ECiQ Immunodiagnostic Systems, the VITROS 3600 Immunodiagnostic System and the VITROS 5600 Integrated System, to aid in the assessment of myocardial damage and risk stratification. Cardiac Troponin I measurement aids in the diagnosis of acute myocardial infarction and in the risk stratification of patients with non-ST-segment elevation acute coronary syndromes with respect to relative risk of mortality, myocardial infarction (MI) or increased probability of ischemic events requiring urgent revascularization procedures.
Indications for Use	• The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI). • The assay can be used as an aid in prognosis for all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS).	• The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI). • The assay can be used as an aid in risk stratification of patients with non-ST segment elevation acute coronary syndromes with respect to relative risk of mortality, MI, or increased probability of ischemic events. • The assay can be used to aid in the assessment of myocardial damage.
Methodology	Chemiluminescence	Chemiluminescence
Assay protocol	Sandwich immunoassay	Sandwich immunoassay
Analyte	Cardiac troponin I	Cardiac troponin I
Specimen Type	Serum, lithium-heparin plasma	Serum and plasma (heparin and EDTA)
Lower Limit of Measuring Range	LoQ (2.50 pg/mL)	LoQ (0.012 ng/mL (12 pg/mL))
Measuring Range	2.50–25,000.00 pg/mL (ng/L)	0.012 – 80.0 ng/mL (12-80,000 pg/mL)
Upper 99th Percentile Cutoff	Female-Lithium Heparin: 34.11 pg/mL Male-Lithium Heparin: 53.48 pg/mL Combined-Lithium Heparin: 45.20 pg/mL Female-Serum: 38.64 pg/mL Male-Serum: 53.53 pg/mL Combined-Serum: 45.43 pg/mL **Overall:** 45.20 pg/mL	0.034 ng/mL (34 pg/mL)
Calibration	2-point calibration	3 levels

The VITROS Troponin I ES Assay was selected as the predicate device for the risk stratification indication for use. The comparison table examines similarities and differences between the candidate and predicate devices for this indication for use. The predicate device was selected based on the following information:

- The predicate device is legally marketed (cleared under K062838).
- The intended use includes the use of Cardiac Troponin I measurements to aid in the diagnosis of acute myocardial infarction, as well as an indication for use for risk stratification.
- Both assays are sandwich assays using chemiluminescent technology indicating that they share the same technological characteristics.
- While the predicate device has a wider measuring range, the measuring range for the candidate device is clinically acceptable since critical concentrations for cardiac troponin I (99^{th} percentile values) are at the lower end of the measuring range. Both assays measure concentrations at low levels suitable for cardiac troponin I. As a result, this difference does not raise questions related to safety or effectiveness.
- The candidate device is more sensitive based on the lower limit of the measuring interval as determined by the Limit of Quantitation.
- Although the predicate device was considered a high-sensitivity assay based on the definition available at the time of clearance, the candidate device meets the current definition of a high-sensitivity assay which includes an additional requirement for at least 50% of measurements from healthy individuals used to determine the 99th percentile value to be above the LoD for the device.

Based on this comparison, the performance characteristics of the candidate device are substantially equivalent to the predicate device to support the addition of an indication for use as an aid in prognosis for all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS).

The candidate device is substantially equivalent in principle and performance to the predicate device cleared under K062838, based on the intended use for diagnosis of AMI, as well as a prognosis indication for use, and performance characteristics.

All analytical performance claims for the candidate device remain the same as the device that was previously cleared in K171566. No changes have been made to the physical device. The purpose of this submission is to expand the intended use of the device to include an indication for use to aid in prognosis for all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS).

9. Special Instrument Requirement

The Atellica® IM TnIH assay is for in vitro diagnostic use with the Atellica® IM Analyzer.

The Atellica® IM Analyzer was previously cleared under 510(k) K151792. Please note that the product name associated with this submission is the interim project name of “Trinidad IM System”. The instrument was subsequently assigned the trade name of “Atellica® IM Analyzer”.

10. Special Conditions for Use Statements

The assay is intended to be used by licensed healthcare professionals.

This assay is labeled For Professional Use.

11. Performance Characteristics – Clinical Study

A clinical performance study was performed to establish additional performance claims for the Atellica® IM TnIH assay.

The objective of this study was to evaluate whether a baseline Atellica® IM TnIH result in patients presenting to the emergency department (ED) with signs and symptoms of acute coronary syndrome (ACS) can predict future mortality or adverse cardiac events.

This prognostic risk analysis utilized the same emergency department cohort previously described in K171566. Following enrollment in the study, a detailed symptom history was obtained for each subject. The following information was collected from each subject's medical chart: age, gender, race, ethnicity, body mass index (BMI), current cardiac risk factors, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation estimate glomerular filtrate rate (eGFR) Interval (mL/min/1.73m^2), concurrent medications, dates of ED admission and discharge, status of ischemic conditions (historically and at ED presentation), and status of acute myocardial infarction (AMI) at initial presentation. Current cardiac risk factors included hypertension, dyslipidemia, diabetes, tobacco use, and depressed left ventricular ejection fraction (LVEF). Ischemic conditions included myocardial infarction (MI), heart failure, and revascularization procedures (percutaneous coronary intervention or coronary artery bypass grafting surgery).

Patients presenting to the emergency department with signs and symptoms suggestive of ACS were followed up for 30-, 90-, 182-, and 365-day progression to ACM and MACE (consisting of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization). At each time point, the risk (cumulative incidence) and hazard ratios were calculated for populations with baseline cTnI levels ≤ or > the overall 99th percentile value. Kaplan-Meier curves were generated to display the absolute risk (cumulative incidence) of ACM and MACE outcomes. Analyses were performed for both serum and lithium heparin plasma sample types using the overall 99th percentile value. The following tables present pre- and post-test risk and unadjusted hazard ratios, adjusted hazard ratios, multivariable Cox proportional hazards (PH) model parameters, and event types, as well as Kaplan-Meier curves, for the following populations based on the overall 99th percentile value:

- Population 1: Entire Population Excluding Subjects with Adjudicated AMI
- Population 2: Entire Population Excluding Subjects with Adjudicated AMI as well as History of Incident or Prior MACE
- Population 3: Entire Population Excluding Subjects with Adjudicated AMI and Including those with History of Incident or Prior MACE

For Populations 1 and 3, results are shown for lithium heparin plasma samples. Similar results were observed for serum samples. For population 2, results are shown for lithium heparin plasma and serum samples. Confidence intervals were generated in accordance with CLSI EP12-Ed3.

Population 3: Entire Population Excluding Subjects with Adjudicated AMI and Including those with History of Incident or Prior MACE

Pre- and Post-Test Risks and Unadjusted Hazard Ratios using the Overall 99th Percentile Value for Population 3

Follow-Up Time Points	Prevalence of ACM/MACE			Risk of ACM/MACE for patients with cTnI levels >99th Percentile			Risk of ACM/MACE for patients with cTnI levels ≤99th Percentile			Unadjusted Hazard Ratio (95% CI)[a]
	Total Number of Patients	Number of ACM/MACE events	Pre-test risk of ACM/MACE (%)	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI[b])	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI)	
30 Days	874	58	6.6	137	13	9.5[d] (5.9, 14.8)	737	45	6.1[d] (5.3, 7.0)	1.61 (0.87, 2.98)[c]
90 Days	874	129	14.8	137	36	26.3 (20.4, 33.2)	737	93	12.6 (11.4, 13.9)	2.24 (1.52, 3.29)
182 Days	874	190	21.7	137	49	35.8 (29.0, 43.2)	737	141	19.1 (17.8, 20.5)	2.09 (1.51, 2.90)
365 Days	874	259	29.6	137	67	48.9 (41.4, 56.4)	737	192	26.1 (24.6, 27.6)	2.21 (1.67, 2.92)

[a] Univariate Cox Proportional Hazards Regression Analysis.
[b] CI = Confidence Interval.
[c] Not Statistically Significant (based on 95% CI)
[d] Difference in post-test risks not statistically significant

Adjusted Hazard Ratios for Population 3

Follow-Up Time Point	N[a]	Adjusted Hazard Ratio (95% CI) [b,c]
30 Days	799	1.07 (0.54, 2.09)[d]
90 Days	799	1.61 (1.06, 2.45)
182 Days	799	1.59 (1.12, 2.26)
365 Days	799	1.56 (1.15, 2.12)

[a] Number of patient samples tested.
[b] Adjusted for prior revascularization, prior heart failure, estimated glomerular filtration rate (eGFR), hypertension, and gender. In this data set, smoking, diabetes, BMI, race, and age were also evaluated and were not significantly associated with cumulative ACM/MACE statistically. Prior MI, statins, and LVEF were evaluated and removed from the model due to observed multicollinearity.
[c] Cox proportional hazards multivariable regression analysis.
[d] Not Statistically Significant (based on 95% CI)

Summary of Multivariable Cox PH Model Parameters for Population 3

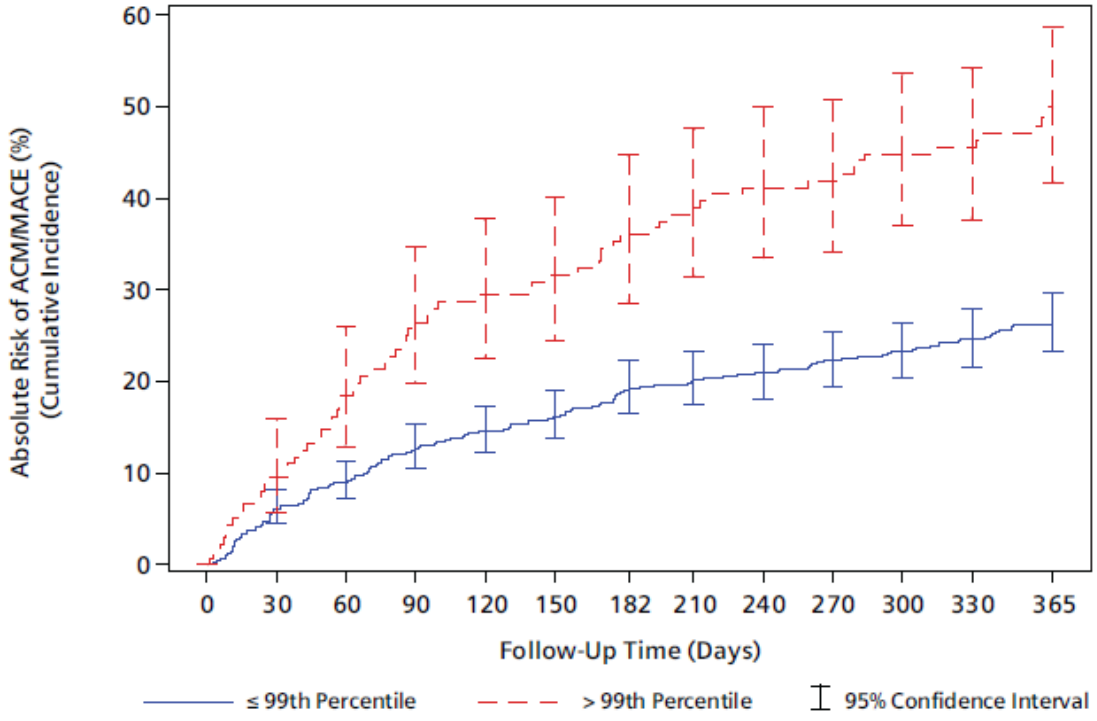
	Adjusted Hazard Ratios (95% CI[a])					
Follow-Up Time Point	cTnI	Prior Revascularization	Prior Heart Failure	eGFR	Hypertension	Gender
30 days	1.07 (0.54, 2.09)[b]	0.64 (0.36, 1.12)[b]	1.76 (0.96, 3.22)[b]	1.59 (0.91, 2.79)[b]	1.16 (0.49, 2.73)[b]	1.62 (0.89, 2.96)[b]
90 days	1.61 (1.06, 2.45)	0.82 (0.56, 1.19)[b]	2.20 (1.45, 3.32)	1.52 (1.05, 2.22)	1.57 (0.82, 3.01)[b]	1.42 (0.96, 2.11)[b]
182 days	1.59 (1.12, 2.26)	0.91 (0.67, 1.24)[b]	2.19 (1.57, 3.04)	1.41 (1.03, 1.92)	1.61 (0.95, 2.74)[b]	1.28 (0.93, 1.75)[b]
365 days	1.56 (1.15, 2.12)	0.91 (0.70, 1.19)[b]	2.23 (1.68, 2.97)	1.50 (1.15, 1.96)	1.54 (0.98, 2.42)[b]	1.28 (0.98, 1.68)[b]

[a] CI = Confidence Interval
[b] Not Statistically Significant (based on 95% CI)

Event Types Summary using the Overall 99th Percentile Value for Population 3

Type of Event	Total, N=874 (%)	≤99th Percentile, N=737 (%)	>99th Percentile, N=137 (%)
Survived to day 365 with no ACM/MACE	606	537	69
Censor (Loss to follow-up)	9	8	1
ACM/MACE	259	192	67
Breakdown of ACM/MACE outcomes			
Cardiac Death	10 (3.86)	9 (4.69)	1 (1.49)
HF Hospitalization	163 (62.93)	113 (58.85)	50 (74.63)
Incident Death	8 (3.09)	5 (2.60)	3 (4.48)
MI	17 (6.56)	13 (6.77)	4 (5.97)
MI, HF Hospitalization	2 (0.77)	1 (0.52)	1 (1.49)
MI, Urgent Revas	7 (2.70)	7 (3.65)	0 (0.00)
MI, Urgent Revas, HF Hospitalization	1 (0.39)	1 (0.52)	0 (0.00)
Other Death	26 (10.04)	19 (9.90)	7 (10.45)
Urgent Revas	24 (9.27)	23 (11.98)	1 (1.49)
Urgent Revas, HF Hospitalization	1 (0.39)	1 (0.52)	0 (0.00)

Kaplan-Meier Curves for Population 3



	Number at Risk												
Follow up Time (Days)	**0**	**30**	**60**	**90**	**120**	**150**	**182**	**210**	**240**	**270**	**300**	**330**	**365**
≤ 99th percentile value	737	690	668	641	625	614	590	582	576	566	559	548	365
> 99th percentile value	137	123	111	101	96	93	87	83	80	79	75	74	44

Population 2: Entire Population Excluding Subjects with Adjudicated AMI as well as History of Incident or Prior MACE

Pre- and Post-Test Risks and Unadjusted Hazard Ratios using the Overall 99th Percentile Value for Population 2

Follow-Up Time Points	Prevalence of ACM/MACE			Risk of ACM/MACE for patients with cTnI levels >99th Percentile			Risk of ACM/MACE for patients with cTnI levels ≤99th Percentile			Unadjusted Hazard Ratio (95% CI)[a]
	Total Number of Patients	Number of ACM/MACE events	Pre-test risk of ACM/MACE (%)	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI[b])	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI)	
Lithium Heparin Plasma										
30 Days	1190	9	0.8	53	3	5.7 (2.2, 13.6)	1137	6	0.5 (0.3, 0.8)	10.89 (2.72, 43.53)
90 Days	1190	17	1.4	53	4	7.5 (3.2, 16.7)	1137	13	1.1 (0.9, 1.5)	6.84 (2.23, 20.98)
182 Days	1190	37	3.1	53	7	13.2 (6.9, 23.9)	1137	30	2.6 (2.3, 3.1)	5.28 (2.32, 12.02)
365 Days	1190	58	4.9	53	8	15.1 (8.1, 26.4)	1137	50	4.4 (4.0, 4.9)	3.69 (1.75, 7.79)
Serum										
30 Days	1214	10	0.8	57	2	3.5 (1.0, 11.4)	1157	8	0.7 (0.5, 0.9)	5.08 (1.08, 23.94)
90 Days	1214	19	1.6	57	3	5.3 (1.9, 13.9)	1157	16	1.4 (1.1, 1.7)	3.87 (1.13, 13.28)
182 Days	1214	39	3.2	57	6	10.5 (5.1, 20.5)	1157	33	2.9 (2.5, 3.2)	3.80 (1.59, 9.07)
365 Days	1214	61	5.0	57	7	12.3 (6.2, 22.8)	1157	54	4.7 (4.3, 5.1)	2.75 (1.25, 6.05)

[a] Univariate Cox Proportional Hazards Regression Analysis.
[b] CI = Confidence Interval.

Adjusted Hazard Ratios for Population 2

Follow-Up Time Point	N[a]	Adjusted Hazard Ratio (95% CI) [b,c]
Lithium Heparin Plasma		
30 Days	1169	7.46 (1.65, 33.65)
90 Days	1169	5.58 (1.69, 18.47)
182 Days	1169	3.89 (1.63, 9.30)
365 Days	1169	2.79 (1.28, 6.08)
Serum		
30 Days	1192	2.84 (0.56, 14.38)[d]
90 Days	1192	2.81 (0.78, 10.12)[d]
182 Days	1192	2.71 (1.10, 6.69)
365 Days	1192	2.06 (0.92, 4.64)[d]

[a] Number of patient samples tested.
[b] Adjusted for estimated glomerular filtration rate (eGFR), hypertension, and gender. In this data set, smoking, diabetes, BMI, race, and age were also evaluated and were not significantly associated with cumulative ACM/MACE statistically. Prior MI, statins, and LVEF were evaluated and removed from the model due to observed multicollinearity.
[c] Cox proportional hazards multivariable regression analysis.
[d] Not Statistically Significant (based on 95% CI)

Summary of Multivariable Cox PH Model Parameters for Population 2

	Adjusted hazard ratios (95% CI)			
Follow-Up Time Point	cTnI	eGFR	Hypertension	Gender
Lithium Heparin Plasma				
30 days	7.46 (1.65, 33.65)	2.16 (0.46, 10.08)[b]	2.07 (0.41, 10.54)[b]	1.32 (0.35, 4.94)[b]
90 days	5.58 (1.69, 18.47)	1.73 (0.51, 5.92)[b]	1.21 (0.43, 3.41)[b]	1.52 (0.58, 4.02)[b]
182 days	3.89 (1.63, 9.30)	2.41 (1.09, 5.33)	1.18 (0.58, 2.40)[b]	1.56 (0.81, 3.00)[b]
365 days	2.79 (1.28, 6.08)	2.30 (1.21, 4.40)	1.20 (0.69, 2.09)[b]	1.53 (0.90, 2.58)[b]
Serum				
30 days	2.84 (0.56, 14.38)[b]	4.05 (1.05, 15.68)	2.28 (0.46, 11.30)[b]	1.52 (0.43, 5.40)[b]
90 days	2.81 (0.78, 10.12)[b]	2.49 (0.84, 7.38)[b]	1.41 (0.52, 3.85)[b]	1.43 (0.57, 3.57)[b]
182 days	2.71 (1.10, 6.69)	2.89 (1.37, 6.08)	1.26 (0.63, 2.53)[b]	1.49 (0.78, 2.82)[b]
365 days	2.06 (0.92, 4.64)[b]	2.61 (1.41, 4.84)	1.19 (0.69, 2.05)[b]	1.52 (0.91, 2.53)[b]

[a] CI = Confidence Interval
[b] Not Statistically Significant (based on 95% CI)

Event Types Summary using the Overall 99th Percentile Value for Population 2

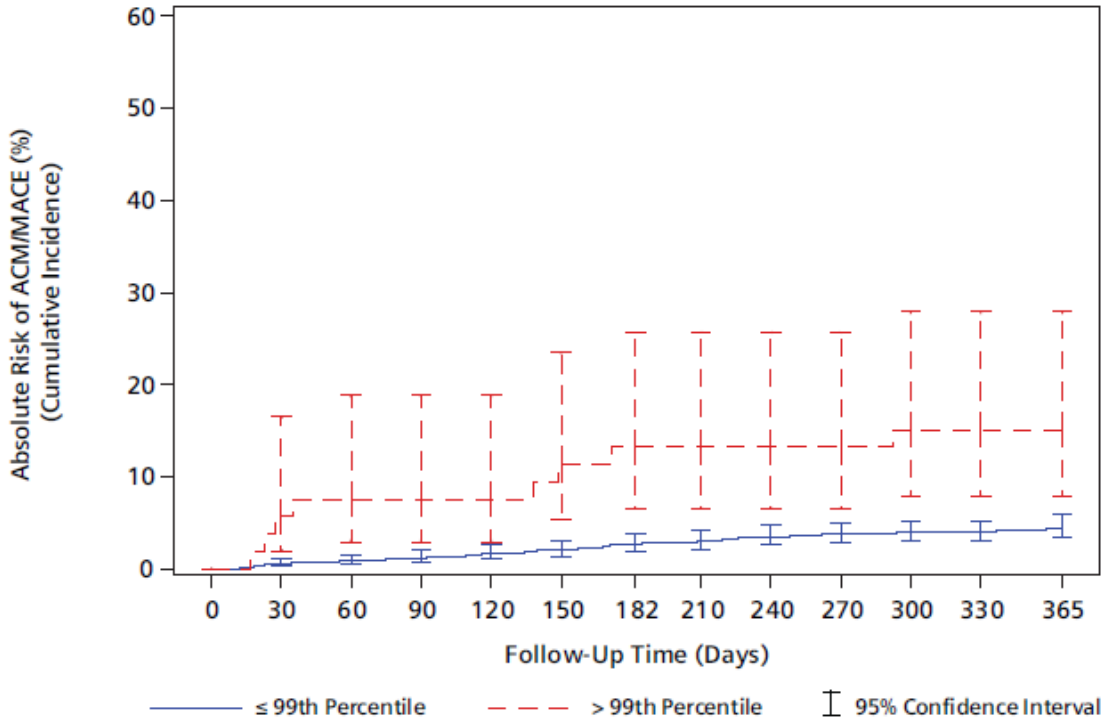
Lithium Heparin Plasma

Type of Event	Total, N=1190 (%)	≤99th Percentile, N=1137 (%)	>99th Percentile, N=53 (%)
Survived to day 365 with no ACM/MACE	1118	1073	45
Censor (Loss to follow-up)	14	14	0
ACM/MACE	58	50	8
Breakdown of ACM/MACE outcomes			
Cardiac Death	2 (3.45)	2 (4.00)	0 (0.00)
HF Hospitalization	29 (50.00)	23 (46.00)	6 (75.00)
MI	4 (6.90)	3 (6.00)	1 (12.50)
MI, Urgent Revas, Cardiac Death	1 (1.72)	0 (0.00)	1 (12.50)
Other Death	14 (24.14)	14 (28.00)	0 (0.00)
Urgent Revas	8 (13.79)	8 (16.00)	0 (0.00)

Serum

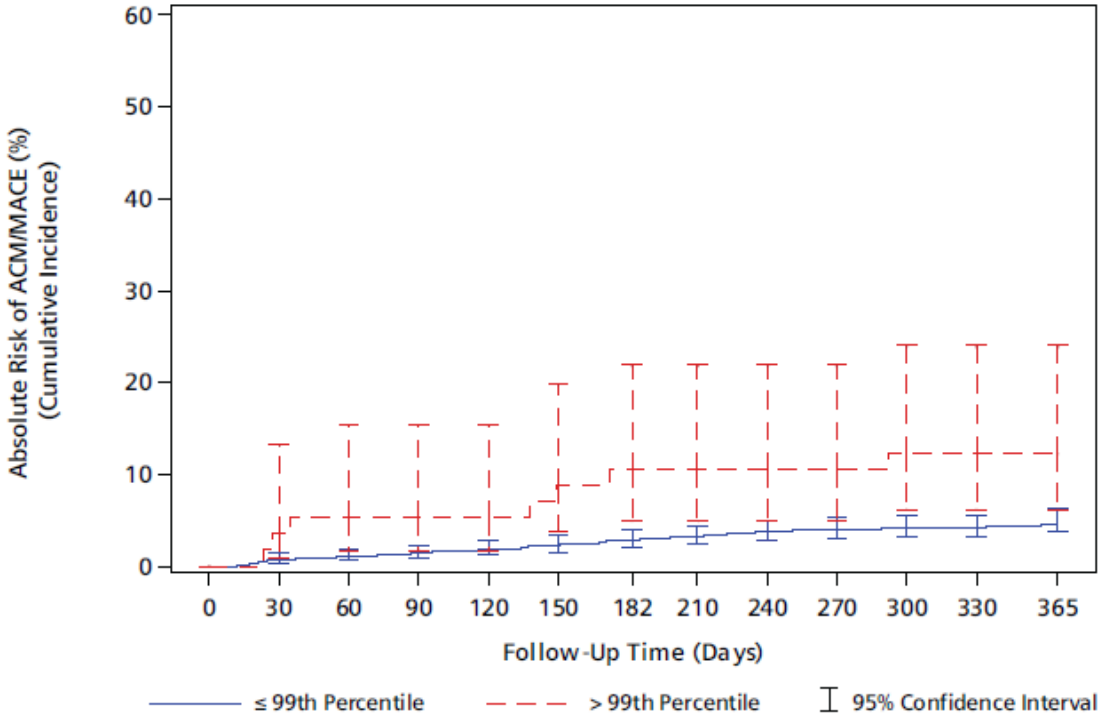
Type of Event	Total, N=1214	≤99th Percentile, N=1157	>99th Percentile, N=57
Survived to day 365 with no ACM/MACE	1139	1089	50
Censor (Loss to follow-up)	14	14	0
ACM/MACE	61	54	7
Breakdown of ACM/MACE event			
Cardiac Death	2 (3.28)	2 (3.70)	0 (0.00)
HF Hospitalization	31 (50.82)	26 (48.15)	5 (71.43)
MI	4 (6.56)	3 (5.56)	1 (14.29)
MI, Urgent Revas, Cardiac Death	1 (1.64)	0 (0.00)	1 (14.29)
Other Death	14 (22.95)	14 (25.93)	0 (0.00)
Urgent Revas	9 (14.75)	9 (16.67)	0 (0.00)

Kaplan-Meier Curves for Population 2
Lithium Heparin Plasma



	Number at Risk												
Follow up Time (Days)	0	30	60	90	120	150	182	210	240	270	300	330	365
≤ 99th percentile value	1137	1128	1120	1113	1107	1103	1095	1090	1084	1081	1079	1078	742
> 99th percentile value	53	50	49	49	49	47	46	46	46	46	45	45	30

Serum



	Number at Risk												
Follow up Time (Days)	**0**	**30**	**60**	**90**	**120**	**150**	**182**	**210**	**240**	**270**	**300**	**330**	**365**
≤ 99th percentile value	1157	1146	1137	1130	1124	1120	1112	1106	1100	1097	1095	1094	748
> 99th percentile value	57	55	54	54	54	52	51	51	51	51	50	50	33

Pre- and Post-Test Risks and Unadjusted Hazard Ratios using the Overall 99th Percentile Value for Population 1

Follow-Up Time Points	Prevalence of ACM/MACE			Risk of ACM/MACE for patients with cTnI levels >99th Percentile			Risk of ACM/MACE for patients with cTnI levels ≤99th Percentile			Unadjusted Hazard Ratio (95% CI)[a]
	Total Number of Patients	Number of ACM/MACE events	Pre-test risk of ACM/MACE (%)	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI[b])	Total Number of Patients	Number of ACM/MACE events	Post-test risk of ACM/MACE (%, 95% CI)	
30 Days	2064	67	3.2	190	16	8.4 (5.5, 12.6)	1874	51	2.7 (2.4, 3.1)	3.21 (1.83, 5.64)
90 Days	2064	146	7.1	190	40	21.1 (16.4, 26.6)	1874	106	5.7 (5.1, 6.2)	4.03 (2.80, 5.80)
182 Days	2064	227	11.0	190	56	29.5 (24.0, 35.6)	1874	171	9.1 (8.5, 9.8)	3.66 (2.71, 4.95)
365 Days	2064	317	15.4	190	75	39.5 (33.3, 46.0)	1874	242	12.9 (12.2, 13.6)	3.64 (2.81, 4.72)

[a] Univariate Cox Proportional Hazards Regression Analysis.
[b] CI = Confidence Interval.

Adjusted Hazard Ratios for Population 1

Follow-Up Time Point	N[a]	Adjusted Hazard Ratio (95% CI) [b,c]
30 Days	1968	1.55 (0.84, 2.89)[d]
90 Days	1968	2.03 (1.36, 3.01)
182 Days	1968	1.97 (1.42, 2.73)
365 Days	1968	1.85 (1.39, 2.47)

[a] Number of patient samples tested.
[b] Adjusted for prior revascularization, prior heart failure, estimated glomerular filtration rate (eGFR), hypertension, and gender. In this data set, smoking, diabetes, BMI, race, and age were also evaluated and were not significantly associated with cumulative ACM/MACE statistically. Prior MI, statins, and LVEF were evaluated and removed from the model due to observed multicollinearity.
[c] Cox proportional hazards multivariable regression analysis.
[d] Not Statistically Significant (based on 95% CI)

Summary of Multivariable Cox PH Model Parameters for Population 1

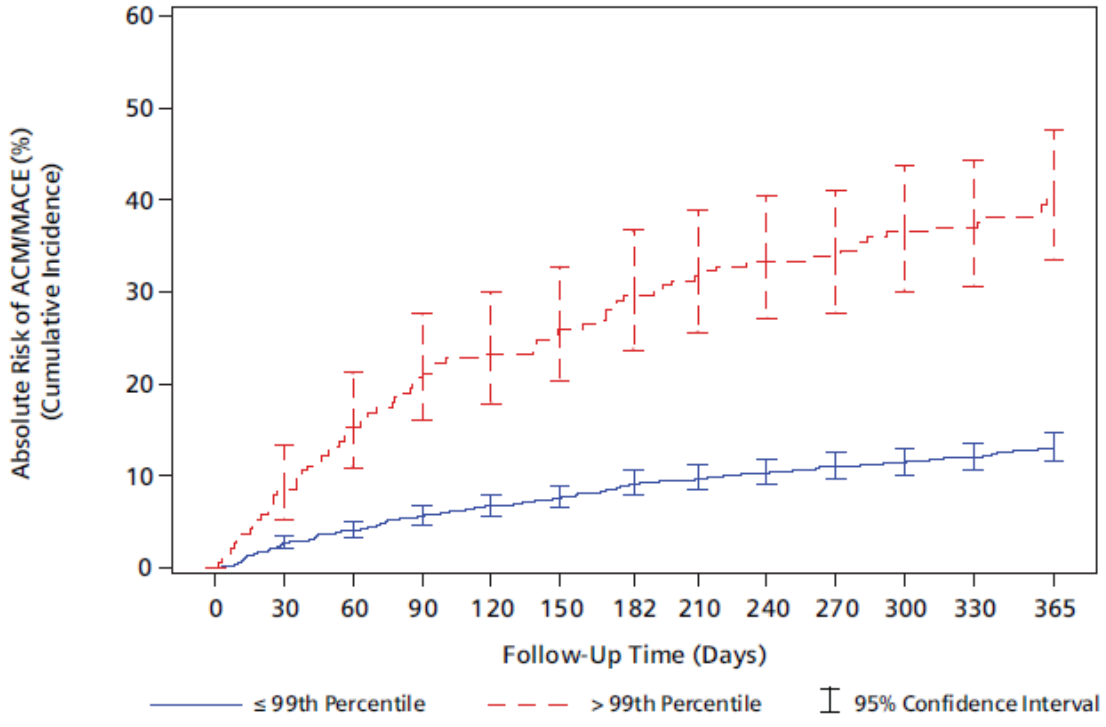
	Adjusted hazard ratios (95% CI[a])					
Follow-Up Time Point	cTnI	Prior Revascularization	Prior Heart Failure	eGFR	Hypertension	Gender
30 days	1.55 (0.84, 2.89)[b]	1.19 (0.71, 2.02)[b]	3.62 (2.07, 6.33)	1.74 (1.02, 2.98)	1.87 (0.86, 4.05)[b]	1.62 (0.94, 2.79)[b]
90 days	2.03 (1.36, 3.01)	1.39 (0.98, 1.97)[b]	4.35 (2.96, 6.38)	1.60 (1.11, 2.29)	1.93 (1.12, 3.31)	1.48 (1.03, 2.14)
182 days	1.97 (1.42, 2.73)	1.50 (1.13, 1.98)	3.79 (2.80, 5.12)	1.56 (1.16, 2.08)	1.85 (1.23, 2.80)	1.37 (1.03, 1.82)
365 days	1.85 (1.39, 2.47)	1.47 (1.16, 1.88)	3.80 (2.94, 4.92)	1.63 (1.27, 2.10)	1.75 (1.24, 2.45)	1.37 (1.08, 1.74)

[a] CI = Confidence Interval
[b] Not Statistically Significant (based on 95% CI)

Event Types Summary using the Overall 99th Percentile Value for Population 1

Type of Event	Total, N=2064 (%)	≤99th percentile, N=1874 (%)	>99th percentile, N=190 (%)
Survived to day 365 with no ACM/MACE	1724	1610	114
Censor (Loss to follow-up)	23	22	1
ACM/MACE	317	242	75
Breakdown of ACM/MACE outcomes			
Cardiac Death	12 (3.79)	11 (4.55)	1 (1.33)
HF Hospitalization	192 (60.57)	136 (56.20)	56 (74.67)
Incident Death	8 (2.52)	5 (2.07)	3 (4.00)
MI	21 (6.62)	16 (6.61)	5 (6.67)
MI,HF Hospitalization	2 (0.63)	1 (0.41)	1 (1.33)
MI, Urgent Revas	7 (2.21)	7 (2.89)	0 (0.00)
MI, Urgent Revas, Cardiac Death	1 (0.32)	0 (0.00)	1 (1.33)
MI, Urgent Revas, HF Hospitalization	1 (0.32)	1 (0.41)	0 (0.00)
Other Death	40 (12.62)	33 (13.64)	7 (9.33)
Urgent Revas	32 (10.09)	31 (12.81)	1 (1.33)
Urgent Revas, HF Hospitalization	1 (0.32)	1 (0.41)	0 (0.00)

Kaplan-Meier Curves for Population 1



	Number at Risk												
Follow up Time (Days)	0	30	60	90	120	150	182	210	240	270	300	330	365
≤ 99th percentile value	1874	1818	1788	1754	1732	1717	1685	1672	1660	1647	1638	1626	1107
> 99th percentile value	190	173	160	150	145	140	133	129	126	125	120	119	74

12. Conclusion

The Atellica® IM High-Sensitivity Troponin I (TnIH) assay is substantially equivalent in principle and performance to the currently marketed predicate device, the VITROS Troponin I ES Assay (K062838). The results of the clinical study provided in this submission support the addition of an indication for use as an aid in prognosis for all-cause mortality (ACM) and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome (ACS).