510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K253539

B Applicant

Axis-Shield Diagnostics Limited

C Proprietary and Established Names

Alere NT-proBNP for Alinity i

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NBC	Class II	21 CFR 862.1117 - B-Type Natriuretic Peptide Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Expansion of Indications for Use

B Measurand:

NT-proBNP

C Type of Test:

Quantitative immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Alere NT-proBNP for Alinity i assay is a chemiluminescent microparticle immunoassay (CMIA) used for the in vitro quantitative determination of N-terminal pro B-type natriuretic peptide (NT-proBNP) in human serum and plasma on the Alinity i system.

The Alere NT-proBNP for Alinity i assay can also be used as an aid in 12-month risk stratification for prognosis of all-cause mortality, cardiac-related mortality, and heart-related hospitalization in patients presenting to the emergency department, diagnosed with new onset or worsening HF.

The assay may further be used in the risk stratification of patients with acute coronary syndrome (ACS).

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

Alinity i system

IV Device/System Characteristics:

A Device Description:

Unchanged since K241176

B Principle of Operation:

Unchanged since K241176

V Substantial Equivalence Information:

A Predicate Device Name(s):

Elecsys ProBNP II Stat Immunoassay

B Predicate 510(k) Number(s):

K092649

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251440	K092649
Device Trade Name	Alere NT-proBNP for Alinity i	Elecsys proBNP II STAT Immunoassay
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the in vitro quantitative determination of N-terminal pro B-type natriuretic peptide (NT-proBNP) in human serum and plasma. This assay may be used in the risk stratification of patients with acute coronary syndrome (ACS).	Same
Specimen Type	Human serum and plasma	Same
Test Principle	Sandwich immunoassay	Same
Measurement Type	Quantitative	Same
Detection Technology	Chemiluminescence	Same
General Device Characteristic Differences		
Principle of Operation	Chemiluminescent microparticle immunoassay (CMIA)	Electro chemiluminescent microparticle immunoassay (ECLIA)
Measuring Interval	15.8 to 35,000.0 pg/mL	5 to 35,000 pg/mL
Hook Effect	No hook effect up to 372,620 pg/mL	No hook effect up to 300,000 pg/mL

VI Standards/Guidance Documents Referenced:

CLSI EP32-R (Formerly X05-R): Metrological Traceability and Its Implementation; A Report

CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Unchanged since K241176.

2. Linearity:

   Unchanged since K241176.

3. Analytical Specificity/Interference:

   Unchanged since K241176.

4. Detection Limit and Assay Reportable Range:

   Unchanged since K241176.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Unchanged since K241176.

6. Assay Cut-Off:

   Unchanged since K241176.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable.

2. Matrix Comparison:

   Unchanged since K241176.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off:

   See "Other Clinical Supportive Data (When 1. and 2. Are Not Applicable)".

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

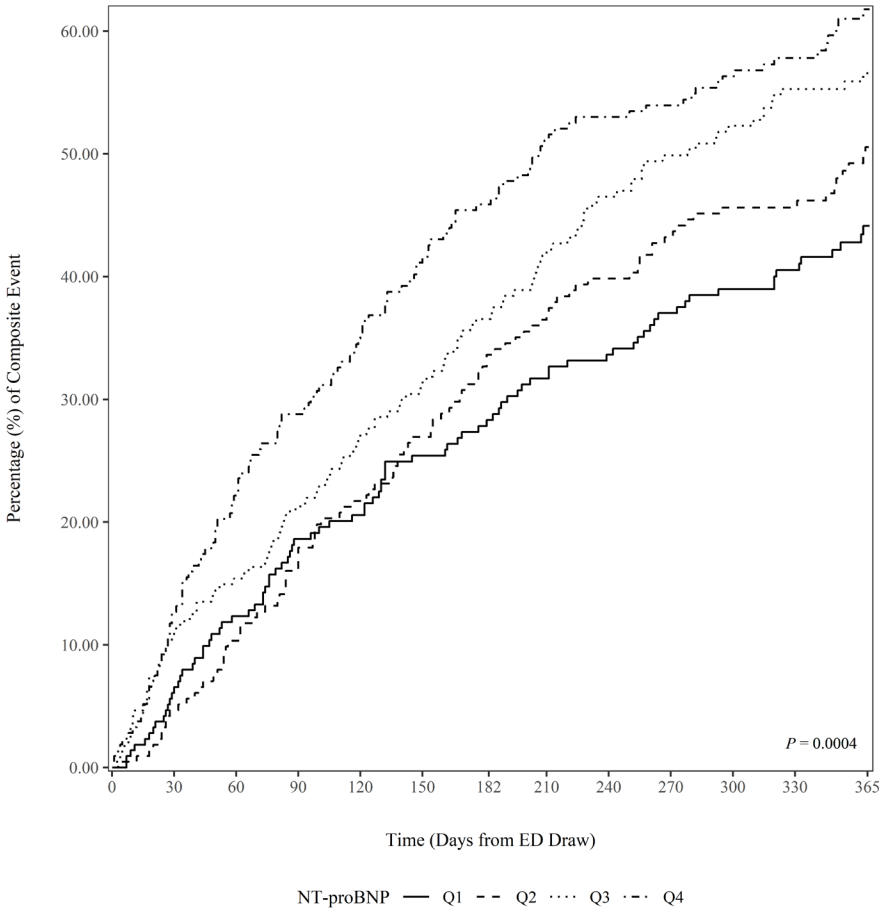
   Risk of Adverse Events in Patients Diagnosed with New Onset or Worsening HF Presenting to the ED

   A clinical study was performed to evaluate the candidate device as an aid in 12-month risk stratification for prognosis of all-cause mortality, cardiac-related mortality, and heart-related hospitalization in patients presenting to the emergency department, diagnosed with new onset or worsening HF using the adjudicated cohort described in K241176. Of the 880 subjects with an adjudicated diagnosis, 861 were prospectively followed for 6±1 and 12±2 months after the initial ED admission. (The remaining 19 subjects did not have a follow-up evaluation.) The study included 495 (57.5%) male subjects and 366 (42.5%) female subjects, with an overall mean age of 62.0 years. Specimens were collected at admission to the ED and tested with the Alere NT-proBNP for Alinity i assay. Study population quartiles for NT-proBNP were calculated in pg/mL from the included population (n = 861):

Study Population Quartile	First Quartile (Q1)	Second Quartile (Q2)	Third Quartile (Q3)	Fourth Quartile (Q4)
NT-proBNP Concentration (pg/mL)	≤ 1214.7	> 1214.7 to 3261.3	> 3261.3 to 7031.3	> 7031.3

   The primary outcome was a composite outcome, defined as the first occurrence of all-cause mortality, cardiac-related mortality, or heart-related hospitalization. The secondary outcomes included the individual components of the composite outcome. The prognostic value of NT-proBNP quartiles was assessed via Kaplan-Meier survival analysis, Cox proportional hazards regression, and event rate analysis (absolute risk) for the primary and secondary outcomes.

   Kaplan-Meier Survival Analysis
   The Kaplan-Meier curves demonstrate that the risk of the composite outcome within 12 months is higher for higher NT-proBNP population quartiles.



Absolute Risk

Absolute risk of each outcome at 12 months was estimated using univariable Cox proportional hazards models. All evaluated outcomes (all-cause mortality, cardiac-related mortality, heart-related hospitalization, and the composite) demonstrate an increasing trend across NT-proBNP quartiles. The results are summarized in the following table.

Outcome	**Absolute Risk (%) (95% CI)**			
	Q1	**Q2**	**Q3**	**Q4**
Composite Outcome	44.03 (36.86, 50.39)	49.40 (42.25, 55.66)	56.49 (49.37, 62.60)	63.08 (55.99, 69.02)
Mortality	10.21 (5.97, 14.25)	11.45 (7.03, 15.66)	18.94 (13.41, 24.12)	25.50 (19.33, 31.19)
Cardiac Mortality	2.03 (0.04, 3.97)	6.84 (3.31, 10.24)	7.24 (3.51, 10.83)	15.78 (10.50, 20.75)
Heart-Related Hospitalization	39.69 (32.44, 46.16)	46.74 (39.43, 53.17)	47.89 (40.34, 54.49)	53.41 (45.55, 60.13)

Cox Proportional Hazards Regression

Univariable results and multivariable results are summarized for the composite outcome and each individual outcome in the table below.

Outcome	NT-proBNP Quartile[a]	Unadjusted Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)[b]
Composite	Q2	1.17 (0.89, 1.56)	1.16 (0.86, 1.56)
	Q3	1.43 (1.09, 1.89)	1.44 (1.08, 1.93)
	Q4	1.72 (1.31, 2.25)	1.56 (1.14, 2.12)
All-Cause Mortality	Q2	1.13 (0.63, 2.03)	1.15 (0.63, 2.10)
	Q3	1.95 (1.15, 3.32)	1.89 (1.08, 3.30)
	Q4	2.73 (1.65, 4.53)	2.13 (1.19, 3.80)
Cardiac-Related Mortality	Q2	3.46 (1.14, 10.52)	3.69 (1.19, 11.42)
	Q3	3.67 (1.21, 11.15)	3.84 (1.22, 12.04)
	Q4	8.39 (2.96, 23.77)	8.24 (2.66, 25.50)
Heart-Related Hospitalization	Q2	1.25 (0.92, 1.68)	1.23 (0.89, 1.69)
	Q3	1.29 (0.95, 1.75)	1.30 (0.94, 1.80)
	Q4	1.51 (1.12, 2.04)	1.44 (1.02, 2.03)

[a] NT-proBNP Q1 is the reference category for the hazard ratios presented for Q2, Q3, and Q4.

[b] The multivariable model was adjusted for age, sex, BMI, smoking, diabetes mellitus, hypertension, eGFR, and NYHA class. Only subjects with complete data for all covariates (n=816) were included

Risk Stratification of Patients with Acute Coronary Syndrome (ACS)

The sponsor provided information to support the risk stratification of patients with ACS claim based on the following clinical guideline and peer-reviewed literature references:

- Rao SV, O'Donoghue ML, Ruel M, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2025;151:e771–e862.

- Jernberg T, Stridsberg M, Venge P, et al. N-terminal pro brain natriuretic peptide on admission for early risk stratification of patients with chest pain and no ST-segment elevation. *J Am Coll Cardiol* 2002;40(3):437-445.
- James SK, Lindahl B, Siegbahn A, et al. N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease; a Global Utilization of Strategies to Open occluded arteries (GUSTO)-IV substudy. *Circulation* 2003;108(3):275-281.

D Expected Values/Reference Range:

Unchanged since K241176.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.