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

A. 510(k) Number:

k140436

B. Purpose for Submission:

New device

C. Measurand:

Galectin-3

D. Type of Test:

Chemiluminescent microparticle immunoassay

E. Applicant:

Fujirebio Diagnostics, Inc.

F. Proprietary and Established Names:

ARCHITECT Galectin-3 Reagent Kit
ARCHITECT Galectin-3 Calibrators
ARCHITECT Galectin-3 Controls

G. Regulatory Information:

Product	Classification	Regulation	Panel
OSX	Class II	21 CFR 862.1117 B-type natriuretic peptide test system	Clinical Chemistry(75)
JIT	Class II	21 CFR 862.1150 Calibrator	Clinical Chemistry (75)
JJX	Class I, reserved	21 CFR 862.1660 Quality Control Material (assayed and unassayed)	Clinical Chemistry(75)

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use.

2. Indication(s) for use:

   Reagent Kit
   The ARCHITECT Galectin-3 assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of galectin-3 in human serum and EDTA plasma.

   The ARCHITECT Galectin-3 assay may be used in conjunction with clinical evaluation as an aid in assessing the prognosis of patients diagnosed with chronic heart failure (HF). The ARCHITECT Galectin-3 assay is used with the ARCHITECT *i* System with *STAT* protocol capability.

   Calibrators
   The ARCHITECT Galectin-3 Calibrators are for the calibration of the ARCHITECT *i* System when used for the quantitative determination of galectin-3 antigen in human serum and EDTA plasma.

   Controls
   The ARCHITECT Galectin-3 Controls are for the verification of the accuracy and precision of the ARCHITECT *i* System when used for the quantitative determination of galectin-3 in human serum and EDTA plasma.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   Abbott ARCHITECT *i* S2000 SR System STAT protocol

I. Device Description:

The ARCHITECT Galectin-3 assay is a two-step immunoassay for the quantitative determination of galectin-3 in human serum or EDTA plasma using CMIA technology.

In the first step, galectin-3 in the sample is immunoprecipitated with anti-galectin-3 coated paramagnetic microparticles. After washing, anti-galectin-3 acridinium-labeled conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units

(RLUs). A direct relationship exists between the amount of galectin-3 in the sample and the RLUs detected by the ARCHITECT *i* System optics.

The kit is composed of the following:

ARCHITECT Galectin-3 Reagent Kit
The ARCHITECT Galectin-3 Reagent Kit consists of 100 tests. Each kit contains paramagnetic microparticles coated with the anti-galectin-3 rat monoclonal antibody, and an acridinium-labeled anti-galectin-3 mouse monoclonal antibody conjugate.

MICROPARTICLES Anti-galectin-3 coated microparticles in PBS buffer with protein stabilizers. Minimum concentration: 0.08% solids.

CONJUGATE Anti-galectin-3 acridinium-labeled conjugate in PBS buffer with protein stabilizers. Minimum concentration: 800 ng/mL.

ARCHITECT Galectin-3 Calibrators
The ARCHITECT Galectin-3 Calibrators are used for the calibration of the ARCHITECT Galectin 3 Assay. The calibrator kit is packaged separately. Each calibrator kit contains one bottle each of Calibrators A, B, C, D, E, and F. Calibrators A through F are prepared with artificial matrix. Calibrators B through F contain HeLa cell lysate galectin-3.

The calibrators are at the following approximate concentrations:

Calibrator	Concentration (ng/mL)
CAL A	0.0
CAL B	5.7
CAL C	11.4
CAL D	22.8
CAL E	68.4
CAL F	114.0

ARCHITECT Galectin-3 Controls
The ARCHITECT Galectin-3 Controls are used for the verification of the accuracy and precision of the ARCHITECT Galectin 3 Assay. The control kit is packaged separately. Each control kit contains one bottle each of low, medium, and high control. The Low, Medium, and High Controls are prepared with artificial matrix and contain HeLa cell lysate galectin-3.

The controls are at the following concentrations ranges:

Control	Concentration Target (ng/mL)	Concentration Range (ng/mL)
Low Control	9.1	6.4 – 11.8
Medium Control	20.5	14.4 – 26.7
High Control	74.1	51.9 – 96.3

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BG Medicine, Inc. Galectin-3 Assay

2. Predicate K number(s):

   k093758

3. Comparison with predicate:

Similarities		
	ARCHITECT Galectin-3 (Candidate Device)	**BG Medicine Galectin-3 Assay (Predicate Device) k093758**
Intended Use	Quantitative determination of galectin-3 in human serum and EDTA plasma. ARCHITECT Galectin-3 assay may be used in conjunction with clinical evaluation as an aid in assessing the prognosis of patients diagnosed with chronic heart failure (HF).	same
Analyte	Human galectin-3	same
Antibodies	Anti-galectin-3 Monoclonal	same

Differences		
	ARCHITECT Galectin-3 (Candidate Device)	**BG Medicine Galectin- 3 Assay (Predicate Device) k093758**
Instrument System	ARCHITECT *i* System	None
Principle of Operation	Chemiluminscent Microparticle Immunoassay (CMIA)	Manual Enzyme Linked Immunosorbent Assay (ELISA)
Interpretation of Results	Calibrator Curve	Standard Curve
Cut-off	Galectin-3 cutoff of 17.8 ng/mL	galectin-3 risk categories: • galectin-3 greater than 25.9 ng/mL • galectin-3 between 17.8 and 25.9 ng/mL •galectin-3 less than or equal to 17.8 ng/mL
Type of Specimen	Human Serum or EDTA plasma	plasma
Assay Range	5.5 – 103.1 ng/mL	1.4 – 94.8 ng/mL

	ARCHITECT Galectin-3 Calibrators (Candidate Device)	**BG Medicine Galectin-3 Assay (Predicate Device) k093758**
Intended Use	The ARCHITECT Galectin-3 Calibrators are for the calibration of the ARCHITECT *i* System when used for the quantitative determination of galectin-3 antigen in human serum and EDTA plasma.	same
Concentrations	6 Levels (0.0 – 114.0 ng/mL)	1 Level (12 ng/vial) Serial diluted

	ARCHITECT Galectin-3 Controls (Candidate Device)	BG Medicine Galectin-3 Assay (Predicate Device) k093758
Intended Use	The ARCHITECT Galectin-3 Controls are for the verification of the accuracy and precision of the ARCHITECT *i* System when used for the quantitative determination of galectin-3 in human serum and EDTA plasma.	same
Concentrations	3 Levels (9.1, 20.5, and 74.1 ng/mL)	2 Levels (18.4 and 69 ng/mL)

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

CLSI C28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures: Approved Guideline

Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff

Class II Special Control Guidance Document for B-Type Natriuretic Peptide Premarket Notifications; Final Guidance for Industry and FDA Reviewers. Document issued on: November 30, 2000

L. Test Principle:

The ARCHITECT Galectin-3 assay is a two-step immunoassay for the quantitative determination of galectin-3 in human serum or EDTA plasma using CMIA technology. In the first step, sample and anti-galectin-3 coated paramagnetic

microparticles are combined. Galectin-3 present in the sample binds to the anti-galecin-3 coated microparticles. After washing, anti-galectin-3 acridinium-labeled conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of galectin-3 in the sample and the RLUs detected by the ARCHITECT *i* System optics.

M. Performance Characteristics (if/when applicable):

All performance testing described herein was performed using the ARCHITECT *i* 2000 SR in STAT mode.

1. Analytical performance:
   a. Precision/Reproducibility:

   Precision of the ARCHITECT Galectin-3 assay was evaluated using a 20 day precision study performed in-house according to CLSI EP05-A2 using a panel of pooled samples as follows: native human serum (targeting a low level concentration of galectin-3), native human EDTA plasma and native human serum each (targeting a galectin-3 concentration near 17.8 ng/mL), human EDTA plasma and human serum spiked with HeLa cell lysate galectin-3 each (targeting a high concentration of galectin-3). The ARCHITECT galectin-3 controls were also tested. All samples were tested using 1 reagent kit lot, 2 replicates per run, 2 runs per day for 20 days for a total of 80 measurements.

Test Specimen	Mean (ng/mL)	Within-Run		Between Run		Total Imprecision	
		SD (ng/mL)	%CV	SD (ng/mL)	%CV	SD (ng/mL)	%CV
Serum/ Native Galectin-3	10.7	0.31	2.9	0.00	0.0	0.34	3.2
Serum/ Native Galectin-3	19.9	0.83	4.2	0.00	0.0	0.83	4.2
Serum/ Lysate Galectin-3	87.3	1.37	1.6	0.85	1.0	1.62	1.8
Plasma/ Native Galectin-3	18.3	0.44	2.4	0.24	1.3	0.51	2.8
Plasma/ Lysate Galectin-3	48.4	0.90	1.9	0.00	0.0	0.90	1.9
Low Galectin-3	9.6	0.30	3.2	0.46	4.8	0.55	5.8

Control							
Medium Galectin-3 Control	19.7	0.56	2.8	0.13	0.7	0.68	3.4
High Galectin-3 Control	73.5	1.38	1.9	0.00	0.0	1.60	2.2

The lot-to-lot precision for two lots of the ARCHITECT Galectin-3 assay was evaluated using a 10 day precision study performed in-house based on CLSI EP05-A2 using a panel of pooled samples as follows: native human serum (targeting a low level concentration of galectin-3), native human EDTA plasma and native human serum each (targeting a galectin-3 concentration near 17.8 ng/mL), human EDTA plasma and human serum spiked with HeLa cell lysate galectin-3 each (targeting a high concentration of galectin-3). The ARCHITECT galectin-3 controls were also tested. All samples were tested using 2 reagent kit lots, 2 replicates per run, 2 runs per day for 10 days for a total of 40 measurements.

Test Specimen	Mean (ng/mL)	Between Lots		Total Imprecision	
		SD (ng/mL)	%CV	SD (ng/mL)	%CV
Serum/ Native Galectin-3	10.5	0.11	1.0	0.32	3.0
Serum/ Native Galectin-3	19.7	0.00	0.0	0.66	3.3
Serum/ Lysate Galectin-3	86.8	0.39	0.4	1.52	1.8
Plasma/ Native Galectin-3	18.0	0.11	0.6	0.43	2.4
Plasma/ Lysate Galectin-3	47.7	0.29	0.6	0.80	1.7
Low Galectin-3 Control	9.4	0.00	0.0	0.44	4.7
Medium Galectin-3 Control	19.4	0.00	0.0	0.52	2.7
High Galectin-3 Control	72.4	0.00	0.0	1.56	2.1

b. Linearity/assay reportable range:

Linearity was evaluated in accordance with the CLSI EP-6A guideline using 1 reagent lot and 1 ARCHITECT *i*2000SR System in STAT mode for both serum and plasma types. Serum and EDTA plasma samples with high concentrations of galectin-3 were prepared by spiking each sample type with HeLa cell lysate galectin-3. Twelve samples spanning the linear range of the assay were prepared for serum and plasma each by intermixing. For serum, a low serum sample (treated to remove galectin-3) was intermixed with the spiked high serum sample. For plasma, a low plasma sample (prepared by dilution with CAL A) was intermixed with spiked high plasma sample. A total of 3 replicates were measured for each sample pool.

The cubic model was significant for all analyses based on unweighted regression models. For serum, the test results did not deviate from linearity by more than 9.2%. For plasma, the test results did not deviate from linearity by more than 2.5%.

High Dose Hook Effect: The sponsor demonstrated that there was no high dose hook effect from the concentration of the CAL F calibrator (≈114 ng/mL) to ≈1400 ng/mL.

The studies support the sponsor's claimed linear range of 5.5 ng/mL to 103.1 ng/mL.

The sponsor includes the following limitation in the labeling: Accuracy may be assessed using samples prepared by diluting the ARCHITECT Galectin-3 Calibrator F with the ARCHITECT Galectin-3 Calibrator A.

The sponsor performed studies to support their recommendation that samples can be diluted 1:2.

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

The ARCHITECT Calibrators and Controls are standardized to an internal gravimetric standard. Calibrators and controls are value assigned using primary reference curves and verified using quality control material and pooled panel samples that must meet specifications. The value assignment process was reviewed and found to be acceptable.

Calibrator and Control Stability: The calibrators and controls are stable for 12 months unopened at 2-8°C. The calibrators and controls are stable for 12 months once opened at 2-8°C. The calibrator and control stability protocols were reviewed and found acceptable.

d. Detection limit:

Limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) studies were performed using a protocol based on CLSI EP-17A, Protocols for Determination of Limits of Detection and Limits of Quantitation and analyzed as described below.

LoB Test Protocol
To estimate LoB, 5 blank samples were measured in replicates of 5 on 2 ARCHITECT *i*2000SR systems (STAT mode) for 2 runs per day over 3 days for each of 2 lots yielding 60 measurements per lot.

LoB was defined as the concentration at which there is a 95% probability that the sample is analyte-free and was calculated nonparametrically.

LoD Test Protocol
To estimate LoD, 5 low level samples were measured in replicates of 5 on 2 ARCHITECT *i*2000SR systems (STAT mode) for 2 runs per day over 3 days for each of 2 lots yielding 60 measurements per lot.

LoD was defined based on a β of 0.05 and was calculated nonparametrically.

LoQ Test Protocol
To estimate LoQ, 5 low level samples were measured in replicates of 5 on 2 ARCHITECT *i*2000SR systems (STAT mode) for 2 runs per day over 3 days for each of 2 lots yielding 60 measurements per lot.

The ARCHITECT Galectin-3 assay exhibits a CV of 10% at the claimed LoQ.

LoB = 1.0 ng/mL
LoD = 1.1 ng/mL
LoQ = 2.8 ng/mL

The measuring range of the assay is 5.5 ng/mL to 103.1 ng/mL based on the linear range of the assay (see section M 1.b above).

e. Analytical specificity:

Cross Reactivity

To evaluate cross reactivity due to protein isoforms (enumerated in the following table), the proteins were added to the following pooled samples: 1 serum sample and 2 EDTA plasma samples with concentrations of native galectin-3 of 10-13 ng/mL, and 1 serum sample spiked with recombinant

galectin-3 at a concentration of 10-13 ng/mL, and 2 plasma samples and 2 serum samples spiked with recombinant galectin-3 for a final concentration of ≈26 ng/mL. Control samples were tested in replicates of 6, and test samples were tested in replicates of 3. For each cross reactant tested, cross reactivity was analyzed by comparing the mean of the true value samples (no interferent added) to the test samples (interferent added) and calculated using the following formula: % cross reactivity = [(mean of test sample – mean of true sample)/concentration of interferent] X 100.

Potentially Interfering Substance	**Interferent Concentration**	**% Cross Reactivity**			
		Serum 12.5 ng/mL	**Serum 24.3 ng/mL**	**Plasma 11.1 ng/mL**	**Plasma 25.2 ng/mL**
Galectin-1	500 ng/mL	0.0	-0.1	0.0	0.2
Galectin-2	500 ng/mL	0.1	-0.1	0.0	0.0
Galectn-4	500 ng/mL	0.0	0.1	0.0	0.2
Galectin-7	500 ng/mL	-0.1	0.0	-0.1	-0.1
Galectin-8	500 ng/mL	0.0	-0.1	0.0	0.0
Galectin-9	500 ng/mL	0.0	-0.1	0.0	0.0
Galectin-12	500 ng/mL	0.0	0.0	0.1	-0.1
Collagen I	500 ng/mL	-0.1	0.0	0.0	-0.1
Collagen III	500 ng/mL	0.1	-0.1	-0.1	-0.1

Endogenous Interferents

To evaluate potential interference due to endogenous substances (enumerated in the following table), the interferents were added to the pooled samples targeting galectin-3 at concentrations of 10-13 ng/mL and ≈26 ng/mL for serum and EDTA plasma. The number and specimen type of pooled samples for each interferent is included in the table below. Control samples were tested in replicates of 3, and test samples were tested in replicates of 3. For each substance tested, interference was analyzed by comparing the mean of the true value samples (no interferent added) to the test samples (interferent added) and calculated according to the following formula: % interference = [(mean of test sample – mean of true sample)/mean of true sample] X 100. The concentrations of interferents used in testing are included below. At the testing concentrations, test results exhibited a maximum bias of ±13.6% with most samples within ±10%.

Potentially Interfering Substance	Number of serum samples tested		Number of EDTA plasma samples tested		Interferent Concentration
	Galectin-3 10-13 ng/mL	Galectin-3 ≈26 ng/mL	Galectin-3 10-13 ng/mL	Galectin-3 ≈26 ng/mL	
Bilirubin (Unconjugated)	2	2	2	2	≥ 40 mg/dL
Bilirubin (Conjugated)	2	2	2	2	≥ 40 mg/dL
Hemoglobin	2	2	2	2	≥ 250 mg/dL
Triglycerides	2	2	2	2	≥ 3000 mg/dL
Human Serum Albumin	4	3	2	2	≥ 12 g/dL
Human Gamma Globulin	2	3	3	2	≥ 5 g/dL
Cholesterol	2	2	2	2	≥ 500 mg/dL
Whole Blood Lysate	2	2	2	2	5 mg/dL
Creatinine	2	2	2	2	≥ 5 mg/dL
Rheumatoid Factor	2	2	2	2	800 IU/mL
Human Anti-Mouse Antibodies	2	2	2	2	1000 ng/mL

Exogenous Substances.

A study was performed based on guidance from the CLSI document EP7-A2. Potentially interfering drugs were evaluated to determine whether galectin-3 concentrations were affected when using the ARCHITECT Galectin-3 assay. The drugs listed below were spiked into serum and EDTA plasma samples with galectin-3 concentrations ranging from approximately 15 to 30 ng/mL and 60 to 90 ng/mL. The samples were assayed, and the galectin-3 concentrations of the spiked samples were compared to control samples. The data are summarized in the following table.

Potentially Interfering Drug	Interferent Concentration	Mean% Difference
Acetaminophen	1324 µmol/L	-1.2
Acetylsalicylic Acid	3.62 mmol/L	1.8
Amlodipine	10.6 µmol/L	-0.1
Ampicillin	152µmol/L	-0.8
Ascorbic Acid	342 µmol/L	-0.2
Atenolol	37.6µmol/L	-0.8
Caffeine	308µmol/L	-0.2
Carvedilol	74 µmol/L	1.5
Captopril	23µmol/L	-1.4
Chloramphenicol	155 µmol/L	0.6
Diclofenac	169 µmol/L	-0.4
Digoxin	7.8 nmol/L	-0.8
Diltiazem	576.5 µmol/L	-1.0
Disopyramide	29.5 µmol/L	-1.2

Dopamine	5.87 µmol/L	-0.2
Enalaprilat	0.86 µmol/L	0.3
Furosemide	181 µmol/L	-0.8
Hydrochlorothiazide	20.2 µmol/L	-0.2
Ibuprofen	2425 µmol/L	0.4
Indomethacin	100 µmol/L	-1.0
Lidocaine	51.2 µmol/L	-0.3
Lisinopril	0.74 µmol/L	-1.2
Losartan	130 µmol/L	-0.1
Lovastatin	191 µmol/L	0.2
Methyldopa	71 µmol/L	-0.3
Metoprolol	18.7 µmol/L	-0.1
Naproxen	2170 µmol/L	-1.0
Nifedipine	1156 nmol/L	0.2
Quinidine	37 µmol/L	1.3
Ramipril	14.4 µmol/L	0.2
Spironolactone	1.44 µmol/L	-1.1
Theophylline	222 µmol/L	-0.2
Trasylol	100 KIE/mL	0.9
Verapamil	244 µmol/L	-0.6
Warfarin	32.5 µmol/L	-1.3

f. Assay cut-off:

See Clinical Cutoff below.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable.

b. Matrix comparison:

The sponsor conducted a matrix comparison study to compare matched serum, K_2EDTA plasma, and K_2EDTA plasma gel samples that included 49 samples that spanned the measuring range (4 samples were spiked with exogenous galectin-3). Samples were tested in singlicate and values ranged from 11.7 – 102.8 ng/mL. A regression analysis was performed comparing to serum with the following results:

Sample Type	Slope	Intercept	r^2
SST Serum	0.95	1.46	0.99
K_2EDTA Plasma	1.06	-0.084	0.99
K_2EDTA Plasma gel	1.05	1.36	0.99

3. Clinical studies:

a. Clinical Sensitivity:

See 3 (c) below.

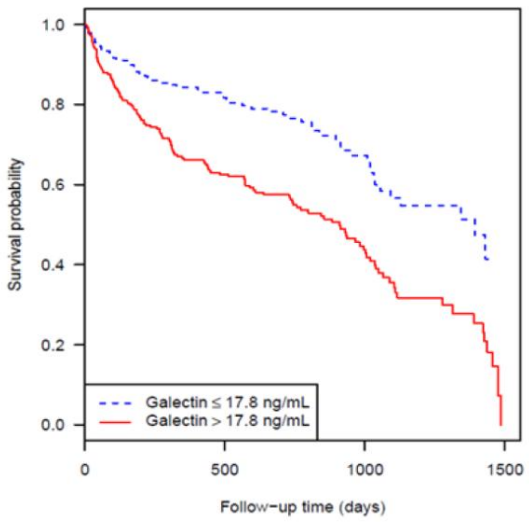
b. Clinical specificity:

See 3 (c) below.

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

The clinical effectiveness at the 17.8 ng/mL cutoff was evaluated using a set of banked serum samples from the Penn Heart Failure study (PHFS). The PHFS is a multi-center prospective cohort study of outpatients with chronic heart failure in the US. The PHFS study population is comprised of approximately 2000 chronic HF patients and includes systolic and diastolic HF patients classified as NYHA class I, II, III, and IV and baseline serum and plasma samples were collected from each subject at enrollment. The study endpoints were all-cause mortality, hospitalization for worsening heart failure, cardiac transplantation and ventricular assist device placement. A study cohort of 405 samples was used to validate the cutoff. The sponsor performed a sensitivity analysis that demonstrated that this study cohort was representative of the whole study. The 17.8 ng/mL cutoff was analyzed using a Cox multi-variate regression model in these 405 patients using the composite of the 4 endpoints. Galectin-3 was significantly associated with increased risk after adjusting for the baseline risk factors of age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes and smoking. The following figures and tables display Kaplan Meier survival curve for all-cause mortality and hazard ratios for the increased risk. The sponsor validated the sample stability of the banked samples.

Kaplan-Meier Survival Curve for Chronic HF Subjects in the Clinical Study

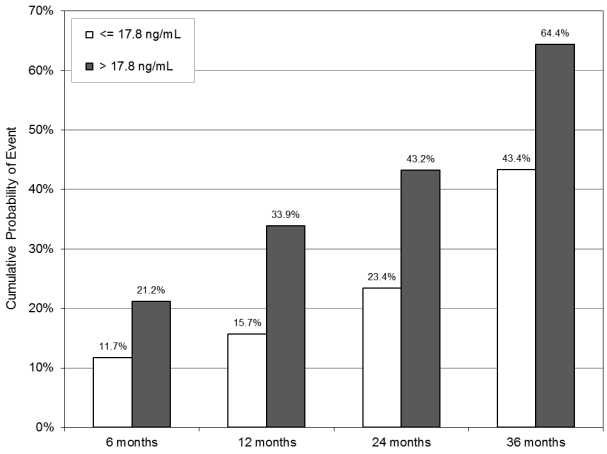


Multi-variate Cox Proportional Hazards Regression Model

Parameter	Hazard Ratio (95% Confidence Interval)	p-value
Galectin-3 > 17.8 ng/mL	1.753 (1.265 – 2.427)	<0.001
Age (per 5 year increment)	1.023 (0.971 – 1.078)	0.396
Gender	1.589 (1.149 – 2.198)	<0.05
NYHA class IV	1.508 (0.625 – 3.638)	0.360
NYHA class III	2.035 (1.248 – 2.334)	<0.01
NYHA class II	1.439 (0.887 – 2.334)	0.140
LVEF (per 10 percent unit increment)	0.835 (0.758 – 0.919)	<0.001
Diabetes	1.049 (0.771 – 1.428)	0.758
Smoker	0.921 (0.576 – 1.472)	0.729

Notation: The reference category for galectin-3 is the lowest galectin-3 (≤17.8 ng/mL). The reference group for gender is female; the reference group for smoker is non-smoker at baseline; the reference group for diabetes is no diabetes at baseline. LVEF and age are included as continuous variables. The reference group for NYHA class is NYHA class I.

The bar graph below depicts the cumulative probability of the primary endpoint (hospitalization due to worsening HF, ventricular assist device placement, cardiac transplantation, or all-cause mortality) by galectin-3 category, at selected time points.



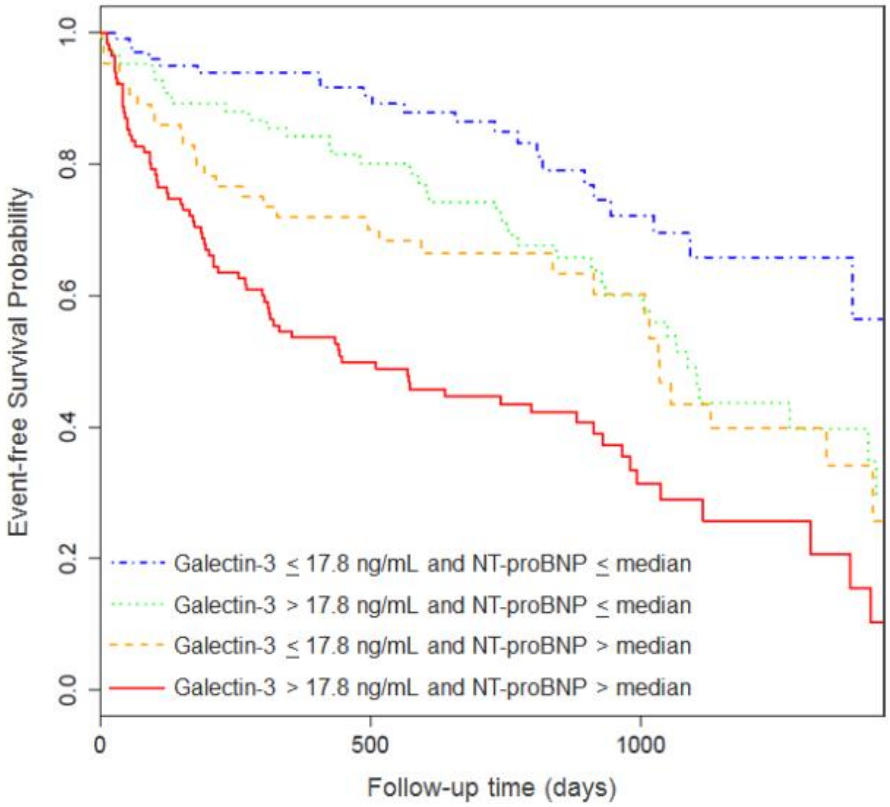
Clinical Interpretation in the context of Natriuretic Peptides

A comparative analysis of galectin-3 concentration, NT-proBNP concentration and event rate using the banked plasma samples from the PHFS was provided to provide additional interpretive information for the clinical use of galectin-3. NT-proBNP was measured at baseline in 361 samples of the 405 samples that validated the clinical cutoff and that were representative of those 405 samples as a whole. The analysis evaluated the event rate for the PHFS composite endpoint in comparison to the concentration of galectin-3 (above and below the cutoff 17.8 ng/mL) and the concentration of NT-proBNP concentrations above and below the median (1222 pg/mL) of the 361 samples that were tested. The sponsor validated the sample stability of the banked samples.

Event Rates by Joint Galectin-3 and NT-proBNP Category

	Subjects In Each Category Experiencing a Hospitalization for Heart Failure, Ventricular Assist Device Placement, Cardiac Transplantation, or Death		
	Percentage of Subjects Experiencing an Event Within Overall Study	Hazard Ratio (95% Confidence Interval)	P-value
Galectin-3 ≤ 17.8 ng/mL and NT-proBNP ≤ median (N=99)	24.2%	1 (referent category)	NA
Galectin-3 ≤ 17.8 ng/mL and NT-proBNP > median (N=64)	48.4%	2.077 (1.216-3.549)	0.007
Galectin-3 > 17.8 ng/mL and NT-proBNP ≤ median (N=83)	48.2%	1.835 (1.104-3.050)	0.019
Galectin-3 > 17.8 ng/mL and NT-proBNP > median (N=115)	66.1%	4.014 (2.533-6.362)	<0.001

Kaplan-Meier Survival Curve by Joint Galectin-3 and NT-proBNP Category in the Clinical Study



4. Clinical cut-off**:**

   See 3 c) above.

   The clinical cutoff of 17.8 ng/mL was predetermined in an independent clinical study

5. Expected values/Reference range:

   The reference range in EDTA plasma was determined in a study according to CLSI C28-A3 using a population of 274 apparently healthy individuals without known heart disease. The study included 136 females and 142 males. This reference population also included individuals from different ethnic backgrounds as follows: 55 African Americans (25 males, 30 females), 9 Asians (4 males, 5 females), 12 Hispanics (9 males, 3 females), 189 Caucasians (97 males, 92 females) and 9 not specified (6 males, 3 females). The distribution of galectin-3 levels is as follows:

Percentile (%)	All (ng/mL)
2.5	8.2
5	9.3
25	12.4
50	14.8
75	18.5
90	22.4
95	25.7
97.5	27.5

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 determination.