BGMEDICINE

510(k) Summary

NOV 17 2010

Company Name:	BG Medicine, Inc.
Address:	610N Lincoln Street Waltham, MA 02451
Telephone:	(781) 405-8772
Fax:	(781) 895-1119
Contact person:	Carol A. Adiletto, M.S.
Date summary prepared:	November 16, 2010

Device Name

Trade Name:	BGM Galectin-3™
Common / Usual name:	Galectin-3 assay
Classification name:	Galectin-3 IVD assay
Product Code:	OSX

Predicate Device

Biosite, Inc. Triage® B-Type Natriuretic Peptide (BNP) Test (K080269, K052789, K051787, K033383, K032235, K030286, K021317, K010266, and K003475).

Device Description

BGM Galectin-3 is a microtiter plate-based sandwich enzyme-linked immunosorbant assay (ELISA) for the quantitative determination of galectin-3 levels in human serum and plasma. BGM Galectin-3 consists of a rat monoclonal anti-mouse galectin-3 antibody coated microtiter plate serving as the solid phase capture antibody and a horseradish peroxidase (HRP)-labeled mouse monoclonal anti-human galectin-3 antibody functioning as the liquid phase tracer antibody for detecting bound galectin-3.

In the testing procedure, galectin-3 in the standard, control, or patient specimen binds to the immobilized capture antibody; after a wash step, bound galectin-3 is detected by the addition of HRP-labeled anti-galectin-3 antibody. Following a second wash step, the presence of bound galectin-3 is demonstrated by an enzymatic blue color development resulting from the addition of tetramethylbenzidene (TMB) solution as the substrate. Color development is stopped by adding sulfuric acid, changing the color to yellow. Color intensity is read at an absorbance of 450 nm using a colorimetric reader. The absorbance is proportional to the galectin-3 levels in the samples, and test results of the samples are determined using a calibration curve derived from the standards.

BGM Galectin-3 contains the microtiter plate, reagents, assayed quality control materials and standards required to perform analyses on serum or EDTA-plasma samples.

Intended Use

BGM Galectin-3 is an *in vitro* diagnostic device that quantitatively measures galectin-3 in serum or EDTA-plasma by enzyme-linked immunosorbant assay (ELISA) on a microtiter plate platform to be used in conjunction with clinical evaluation as an aid in assessing prognosis of patients diagnosed with chronic heart failure (HF). BGM Galectin-3 is indicated for prescription use only.

Table 1. Comparison of Similarities and Differences to Predicate

Comparison Item	Predicate Device *Biosite, Inc. Triage® BNP Test*[1,2]	Subject Device *BGM Galectin-3™*
Intended Use	Quantitative Measurement of B-Type Natriuretic Peptide (BNP)	Quantitative measurement of galectin-3
Indications for Use	An aid in the: ▪ **Risk stratification of patients with heart failure** ▪ Diagnosis of heart failure ▪ Assessment of heart failure severity ▪ Risk stratification of patients with acute coronary syndromes ▪ Diagnostic utility of BNP in patients with heart failure	An aid in: ▪ **Assessing the prognosis of patients with chronic heart failure**
Test Principle	Sandwich ELISA	Sandwich ELISA
Specimen	Whole blood and EDTA-plasma	EDTA-plasma and serum
Analyte	Human B-type natriuretic peptide	Human galectin-3
Antibody	Mouse monoclonal and polyclonal antibodies against BNP, labeled with a fluorescent dye and immobilized on the solid phase, and stabilizers	Two monoclonal antibodies against galectin-3; one immobilized on the solid phase and the other labeled with horseradish peroxidase
Instrument	Fluorometer: either the Triage® Meter or the Beckman Coulter (Access, Access 2, Synchron LXi 725, and UniCel Dxl 800)	Spectrophotometer (plate reader). (Not supplied.) Detection Method: Optical Density at 450 nm
Controls	Triage® BNP Controls	BGM Galectin-3 Quality Control materials

[1] Triage® BNP Test package insert 2234en Rev. E ©2006 Biosite Incorporated
[2] 510(k) summaries from FDA website

Comparison Item	Predicate Device *Biosite, Inc. Triage® BNP Test*	Subject Device *BGM Galectin-3™*
Precision	▪ Average within-day 8.8-11.6 % CV from 71.3-4087.9 pg/mL ▪ Average total 9.9-12.2 % CV from 71.3-4087.9 pg/mL	▪ Within-run imprecision: 2.1-5.7% CV from 6.1-72.2 ng/mL ▪ Total imprecision: 4.2-12.0 % CV from 6.1-72.2 ng/mL
Expected Values (Reference Range)	▪ BNP levels were measured in 1,286 individuals (676 women, 610 men) without CHF using the Triage® BNP Test. ▪ A statistically significant difference between males and females and among age groups is shown. ▪ Descriptive statistics and the 95th percentile are reported for males and females by age category. ▪ A "decision threshold" of 100 pg/mL is recommended for use as an aid in the diagnosis of heart failure indication.	▪ Galectin-3 levels were measured in 1,099 individuals (575 women, 524 men) without heart failure using the BGM Galectin-3 test. ▪ Gender-specific or age category-specific reference intervals were found not to be warranted, per NCCLS (CLSI) guidelines. ▪ Descriptive statistics and percentiles are reported. ▪ Clinical cutoffs were derived in a separate study (see below).
Clinical Study Results	▪ K051787 – FDA Decision Summary states: "In support of the new intended use, the sponsor provided five peer-reviewed articles from the scientific literature assessing the clinical utility of BNP measurements as an aid in the risk stratification of patients with heart failure. All five studies utilized the Biosite Triage BNP device in their test method." ▪ Biosite Triage labeling states: "A systematic review of studies investigating BNP for prognostic utility in patients with heart failure concluded that every 100 pg/mL increase in BNP concentration was associated with a 35% increase in the relative risk of death.	○ Galectin-3 levels were measured in 582 individuals with HF to derive cutoff values: ○ Galectin-3 ≤ 17.8 ng/mL ○ Galectin-3 17.8 – 25.9 ng/mL ○ Galectin-3 > 25.9 ng/mL ▪ A separate study of 895 individuals with HF was conducted in order to validate the proposed cutoff values. ○ Heart failure patients with galectin-3 levels >17.8 ng/mL had a statistically significantly increased hazard of death or hospitalization relative to heart failure patients with levels ≤ 17.8 ng/mL. Elevated galectin-3 levels remained statistically significantly associated with increased hazard after adjustment for other baseline risk factors of age, gender, NYHA class, left ventricular ejection fraction, diabetes status, and smoking status. Levels above 25.9 ng/mL confer a further increase in risk.

Summary of Performance Data

Precision

Precision of BGM Galectin-3 was assessed in an evaluation according to the CLSI EP5-A2 guideline. Six (6) EDTA-plasma pools spanning a range of galectin-3 concentrations were analyzed in duplicate with two (2) runs per day over twenty (20) days using one (1) reagent lot, two (2) operators and one (1) microtiter plate reader. Estimates of within-run, run-to-run, day-to-day and total precision were calculated and met acceptance criteria. Results are summarized in Table 2.

Table 2. Precision of BGM Galectin-3

Test Specimen #	Galectin-3 mean (ng/mL)	Within run		Run to run		Day to day		Total	
		SD	CV%	SD	CV%	SD	CV%	SD	CV%
1	6.1	0.3	5.7	0.6	10.5	0.0	0.0	0.7	12.0
2	17.6	0.4	2.1	0.7	3.8	0.5	2.8	0.9	5.1
3	20.7	0.7	3.4	1.4	6.7	0.3	1.7	1.6	7.7
4	26.3	0.6	2.2	0.8	3.0	0.5	2.1	1.1	4.2
5	46.2	1.1	2.4	1.6	3.6	0.5	1.1	2.0	4.4
6	72.2	2.4	3.3	4.3	6.0	2.9	4.0	5.7	8.0

The table above shows the results of the precision evaluation with EDTA-plasma pools. An additional experiment was performed using serum pools which yielded similar results. Additional test pools at multiple galectin-3 concentrations were also tested and yielded similar results.

Clinical Laboratory Precision

Precision was also evaluated at three (3) CLIA-certified clinical laboratories according the CLSI EP5-A2 guideline. The study included testing of EDTA-plasma pools spanning three (3) galectin-3 concentrations, across two (2) reagent lots, using three (3) different models of microtiter plate readers, and a total of four (4) different operators. Total testing days were 17, 18 and 20 days across the three sites, yielding 110 unique analytical runs. Results from each of the CLIA laboratories were within acceptable limits. Within run and total imprecision estimates are summarized in Table 3.

Table 3. Clinical Laboratory Precision - Within Run and Total Imprecision

CLIA Lab	# days, # runs	Galectin-3 mean (ng/mL)	Within Run		Total	
			SD	CV%	SD	CV%
A	20 days, 40 runs	6.0	0.30	5.0	0.46	7.7
		20.1	0.59	2.9	1.20	6.0
		68.3	2.71	4.0	9.97	14.6
B	17 days, 34 runs	6.7	0.36	5.4	0.63	9.4
		21.6	0.56	2.6	1.55	7.2
		75.5	1.71	2.3	12.75	16.9
C	18 days, 36 runs	6.3	0.46	7.3	0.59	9.4
		21.2	0.71	3.3	1.19	5.6
		71.5	2.16	3.0	6.25	8.7

Linearity

The linearity of BGM Galectin-3 was established according to the recommendations of the Clinical and Laboratory Standards Institute Evaluation Protocol 6 (CLSI EP6-A guideline). Samples were prepared to span a clinically-meaningful measurement range of galectin-3 concentrations. Linearity of BGM Galectin-3 was demonstrated between 1.4 and 94.8 ng/mL. These linearity data are shown in Figure 1.

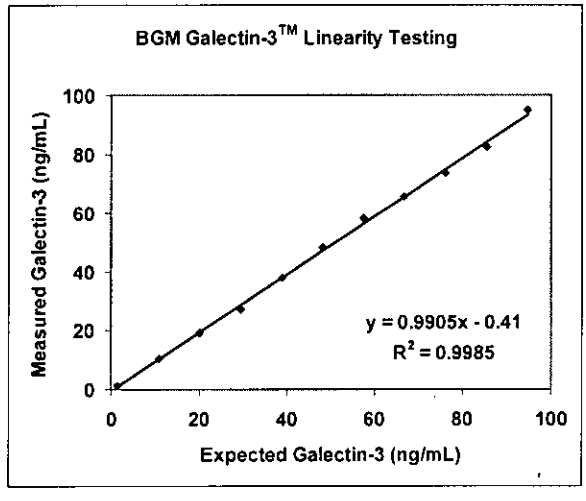

Figure 1: Linearity of BGM Galectin-3

Dilution Parallelism

Dilution parallelism was evaluated by analyzing ten (10) clinical specimens with endogenous native galectin-3 concentrations from 21.6 ng/mL to 88.5 ng/mL at 1:20, 1:40, 1:80 and 1:160 dilutions. Results support ten-fold sample dilution only (1:10). Samples that yield galectin-3 results greater than the upper end of the measurement range (94.8 ng/mL) should NOT be diluted beyond 1:10 and should be reported as "galectin-3 value exceeds the upper limit of the measurement range" or utilize language consistent with laboratory or institutional policies.

High Dose Hook Effect

There is no high dose hook effect at galectin-3 levels up to 500 ng/mL.

Sample Matrices

The BGM Galectin-3 assay has been validated for use with EDTA-plasma or serum samples. The equivalence of these sample matrices were demonstrated in a study of forty-nine (49) matched serum and EDTA-plasma samples with values spanning the measurement range. The regression equation is shown in the x/y scatter plot in Figure 2.

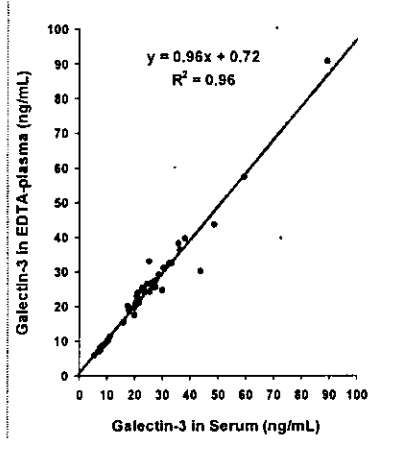

Figure 2: BGM Galectin-3 Serum and EDTA-Plasma Regression

Detection Limit

The limit of detection and limit of quantitation of BGM Galectin-3 were established according to the recommendation of the CLSI EP17-A guideline. The limit of blank (LoB) was determined as the 95th percentile value of forty-eight (48) replicate measurements of the BGM Galectin-3 Assay Buffer. The limit of detection (LoD) was LoD = LoB + c_β SDs, where SDs is the pooled standard deviations from four (4) serum samples with different levels of galectin-3, each of which was measured in sixteen (16) replicates (for a total of sixty-four (64) measurements) and c_β is the 95th percentile of the standard Gaussian distribution corrected for the degree of freedom. The Limit of quantitation (LoQ) was specified as the lowest galectin-3 concentration of the serum samples closest to while above the LoD, which is 1.32 ng/mL. For this sample, the coefficient of variation (CV) for the galectin-3 measurement was 10.4%.

Limit of Blank (LoB):	LoB = 0.86 ng/mL
Limit of Detection (LoD):	LoD = 1.13 ng/mL
Limit of Quantitation (LoQ):	LoQ = 1.32 ng/mL

Note: The LoQ does not represent the lower end of the measuring range and should not be used for that purpose. The measuring range is 1.4 to 94.8 ng/mL as reported in the Measuring Range and Linearity sections of this document.

Cross Reactivity

BGM Galectin-3 displayed no significant cross-reactivity when tested in the presence of the following compounds: galectin-1, galectin-2, galectin-4, galectin-7, galectin-8, galectin-9, galectin-12, collagen I and collagen III, all at a concentration of 500 ng/mL. The mean % cross-reactivity of the above potential cross-reactants is at or below 0.3%.

Interfering Substances

BGM Galectin-3 was evaluated for the effects of potential interfering substances, both endogenous and exogenous, according to the recommendations of the CLSI EP7-A guideline, using an interference acceptance limit of +/-10%. Conjugated bilirubin (up to 16.8 mg/dL), unconjugated bilirubin (up to 40.3 mg/dL), albumin (BSA, up to 12 g/dL), triglycerides (up to 3000 mg/dL), cholesterol (up to 747 mg/dL), and creatinine (up to 5 mg/dL) do not show any significant interference in the assay based on the interference acceptance limit (+/- 10%). Purified hemoglobin (up to 500 mg/dL) does not show significant interference in BGM Galectin-3; however, packed blood cell lysate does show interference. Human anti-mouse antibodies (HAMA) and rheumatoid factor (RF) cause significant positive interference and rheumatoid factor (RF) greater than 50 IU/mL causes significant positive interference with BGM Galectin-3. High levels of gamma globulins ($\geq$ 2.5 g/dL) may cause false elevation in galectin-3 levels. This information is summarized in Table 4.

Table 4. Endogenous Interference Summary

Potential interfering substance	**Result of interference study based on an interference acceptance limit of +/- 10%**
Conjugated bilirubin	No significant interference up to 16.8 mg/dL
Unconjugated bilirubin	No significant interference up to 40.3 mg/dL
Albumin	No significant interference up to 12 g/dL
Triglycerides	No significant interference up to 3000 mg/dL
Cholesterol	No significant interference up to 747 mg/dL
Creatinine	No significant interference up to 5 mg/dL
Purified hemoglobin	No significant interference up to 500 mg/dL
Whole blood lysate	Hemolyzed specimens should not be used with BGM Galectin-3™
Human anti-mouse antibodies (HAMA)	Specimens from patients with HAMA should not be used with BGM Galectin-3™
Rheumatoid Factor (RF)	Interference seen at levels > 50 IU/mL
Gamma globulins	Interference seen at levels ≥ 2.5 g/dL

BGM Galectin-3 measurements were not significantly affected when tested in the presence of thirty-four (34) common pharmaceutical substances; including HF drugs (refer to Table 5). All analytes fall within the interference acceptance limit of +/- 10%.

Table 5: Common Drugs That Did Not Show Interference with BGM Galectin-3

Acetaminophen	Carvèdilol	Dopamine	Lisinopril	Quinidine
Acetylsalicylic acid	Captopril	Enalaprilat	Losartan	Ramipril
Amlodipine	Chloramphenicol	Furosemide	Lovastatin	Spironolactone
Ampicillin	Diclofenac	Hydrochlorothiazide	Methyldopa	Theophylline
Ascorbic Acid	Digoxin	Ibuprofen	Metoprolol	Verapamil
Atenolol	Diltiazem	Indomethacin	Naproxen	Warfarin
Caffeine	Disopyramide	Lidocaine	Nifedipine	

Expected Values (Reference Range)

A reference distribution for galectin-3 was determined through an observational study. Galectin-3 levels were measured in 1,099 banked plasma samples from a population of apparently healthy subjects without known heart disease but that otherwise resemble, by age and gender distribution, the HF patient population. Specimens were from women between the ages of 60 and 80 years (n=575) and men between the ages of 55 and 80 (n=524). This reference population comprised individuals of different ethnic background, as follows: Black or African-American (n=307, 27.9%), Caucasian (n=691, 62.9%), Hispanic (n=42, 3.8%), Asian or Pacific Islander (n=30, 2.7%), and not specified (n=29, 2.6%). All subjects had detectable galectin-3 levels (min-max, 3.2 - 94.6 ng/mL) within the measuring range of BGM Galectin-3. Blood plasma samples were collected from study participant into tubes containing

EDTA. The blood was processed and blood plasma was subsequently frozen at -80°C or colder.

Table 6 summarizes the galectin-3 distribution results. The 97.5th percentile of the galectin-3 distribution from this reference population is 26.2 ng/mL.

Each laboratory should establish a reference range that is representative of the patient population to be evaluated. Additionally, each laboratory should consider their current practice in the evaluation of heart failure patients at each institution.

Table 6. Distribution of Galectin-3 Levels in Subjects without Known Heart Disease

Percentile	Galectin-3 (ng/mL)
2.5th	5.4
5th	6.3
25th	9.7
50th	12.4
75th	15.6
90th	19.0
95th	22.1
97.5th	26.2

Clinical Studies and Interpretation of Results

To validate the clinical effectiveness of the BGM Galectin-3 assay, galectin-3 levels were measured in an independent set of 895 banked EDTA-plasma samples from patients in the United States and Canada in a controlled multi-center clinical study, the Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study. The HF-ACTION study involved 2,331 chronic HF patients with left ventricular dysfunction and with NYHA class II, III or IV symptoms. The average age of the 895 participants whose galectin-3 levels were assessed in the clinical validation study was 58 years, 29% were female, and 36% were non-white. Sensitivity analysis was performed comparing the set of 895 HF-ACTION subjects having evaluable galectin-3 values with all other HF-ACTION participants, and it was found that the clinical validation results based on the evaluable set of subjects were robust and representative of the larger study population. The median follow-up time was approximately 30 months. Participants were categorized based on galectin-3 risk categories defined below:

The derived galectin-3-dependent risk categories are as follows:

- 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

For the clinical validation study, Cox regression models were used to evaluate the association of baseline galectin-3 levels in HF patients with the endpoints of: (i) composite of all-cause mortality and all-cause hospitalization, (ii) cardiovascular mortality, and (iii) composite of cardiovascular mortality and heart failure-related hospitalization, and (iv) all-cause mortality. Galectin-3 levels were found to be significantly associated with increased risk of each of these endpoints in Cox regression models (Table 7, Table 9, Table 11, and Table 14). Galectin-3 remained significantly associated with increased risk upon adjustment for baseline risk factors of age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes status, and smoking status. Figure 3 displays Kaplan Meier curves for the composite endpoint of all-cause mortality or all-cause hospitalization, by baseline galectin-3 category.

Figure 4, Figure 5 and Figure 6 display cumulative probabilities for events for the endpoints of the composite of all-cause mortality and all-cause hospitalization, cardiovascular mortality, and the composite of cardiovascular mortality and heart failure-related hospitalization in the clinical validation study, by baseline galectin-3 category at timepoints of 6, 12, 24 and 36 months after baseline.

All-Cause Mortality and All-Cause Hospitalization

Table 7. Hazard Ratios for All-Cause Mortality and All-Cause Hospitalization Events for HF Subjects in the Clinical Validation Study

	Hazard Ratio (95% CI, p value)		
Galectin-3 Category	≤ 17.8 ng/mL	17.8-25.9 ng/mL	> 25.9 ng/mL
Number of Subjects	647	170	78
Galectin-3*	1.0	1.35 (1.10-1.65, p= 0.004)	1.46 (1.11-1.92, p= 0.006)

**adjusted for baseline risk factors: age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes status, and smoking status.*

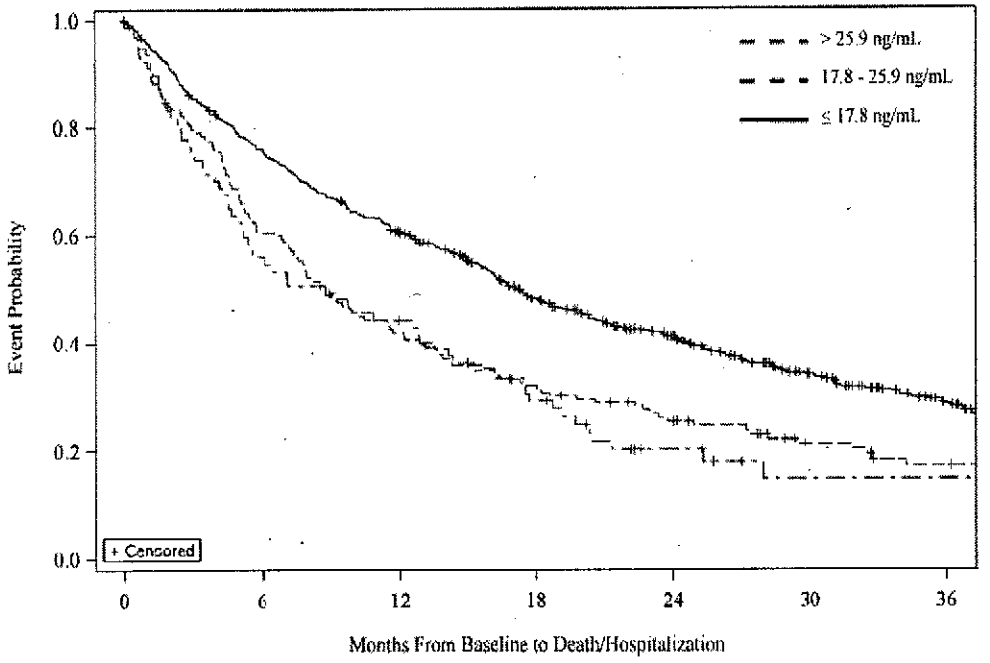

Figure 3: Kaplan-Meier Curves for the Composite Endpoint of All-Cause Mortality or All-Cause Hospitalization, for HF Subjects in the Clinical Validation Study, by Baseline Galectin-3 Level

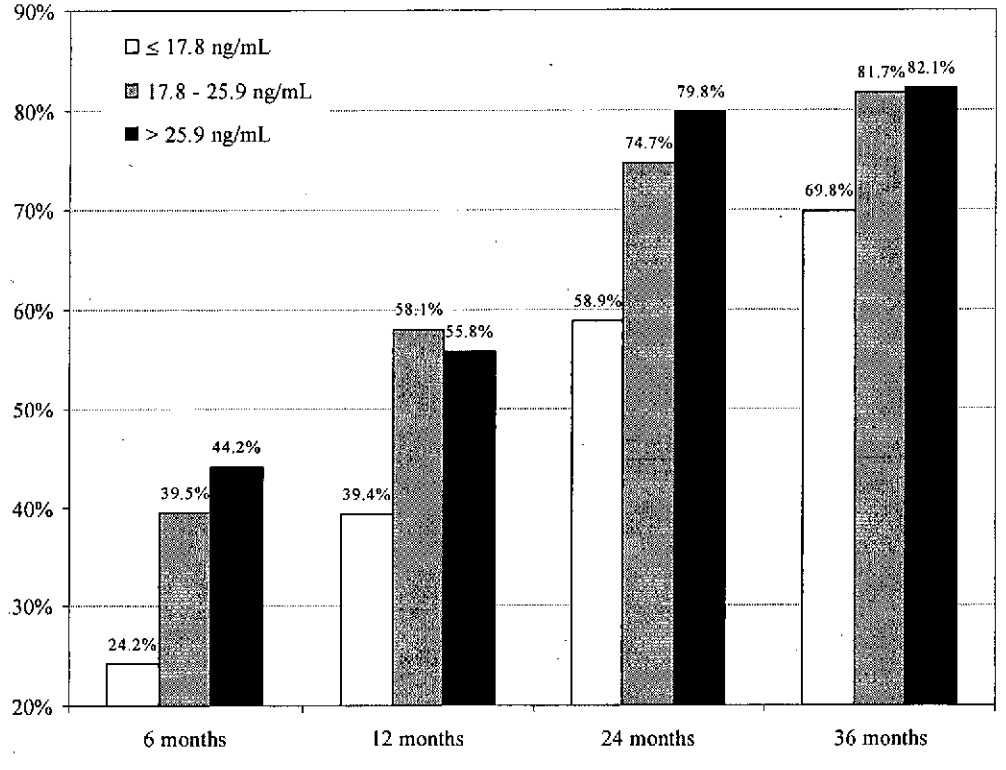

Figure 4: Cumulative Probability of Event for the Composite Endpoint of All-Cause Mortality and All-Cause Hospitalization, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

Table 8. Cumulative Probability (with 95% Confidence Intervals) of Event for the Composite Endpoint of All-Cause Mortality and All-Cause Hospitalization, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

	Cumulative Probability of All-Cause Mortality and All-Cause Hospitalization (95% CI) by Galectin-3 Category and Time Point (in percent)			
Galectin-3 Category	**6 months**	**12 months**	**24 months**	**36 months**
≤ 17.8 ng/mL	24.2% (21.1%-27.7%)	39.4 (35.7-43.3)	58.9 (55.0-62.9)	69.8 (65.8-73.7)
17.8-25.9 ng/mL	39.5 (32.5-47.3)	58.1 (50.8-65.7)	74.7 (67.7-81.1)	81.7 (74.9-87.6)
> 25.9 ng/mL	44.2 (33.9-55.9)	55.8 (45.2-67.1)	79.8 (69.9-88.2)	82.1 (72.0-90.0)

Cardiovascular Mortality

Table 9. Hazard Ratios for Cardiovascular Mortality Events for HF Subjects in the Clinical Validation Study

	Hazard Ratio (95% CI, p value)		
Galectin-3 Category	≤ 17.8 ng/mL	17.8-25.9 ng/mL	> 25.9 ng/mL
Number of Subjects	647	170	78
Galectin-3*	1.0	1.91 (1.28-2.86, p= 0.002)	2.33 (1.43-3.80, p < 0.001)

**adjusted for baseline risk factors: age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes status, and smoking status.*

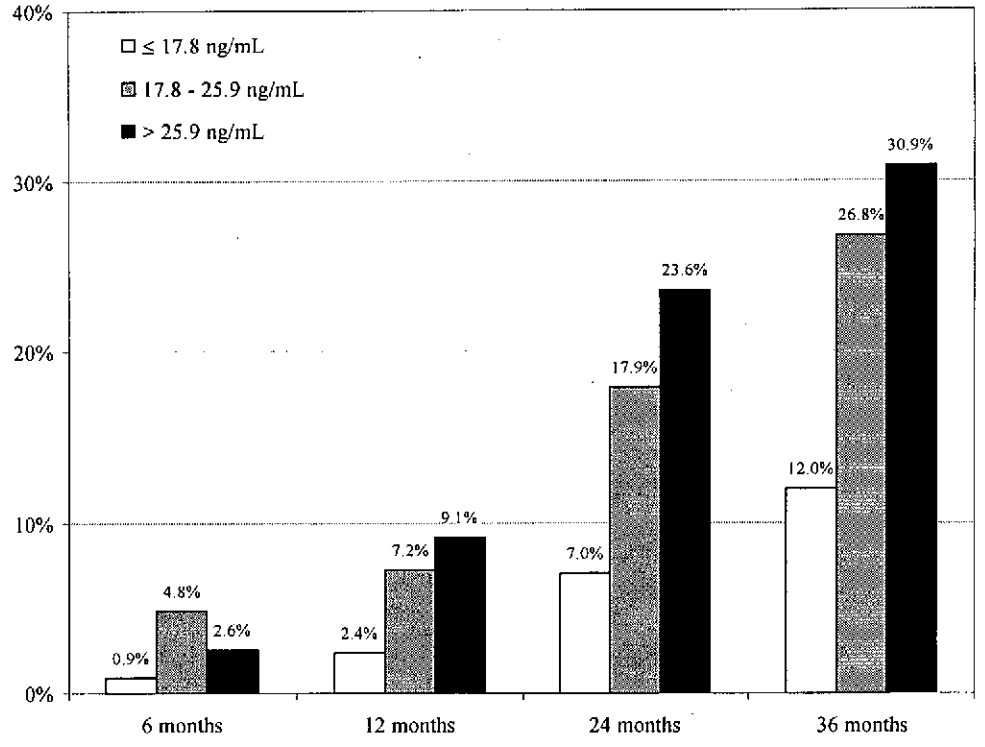

Figure 5: Cumulative Probability of Event for the Endpoint of Cardiovascular Mortality, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

Table 10. Cumulative Probability (with 95% Confidence Intervals) of Event for the Cardiovascular Mortality, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

	Cumulative Probability of Cardiovascular Mortality (95% CI) by Galectin-3 Category and Time Point (in percent)			
Galectin-3 Category	**6 months**	**12 months**	**24 months**	**36 months**
≤ 17.8 ng/mL	0.9% (0.4%-2.1%)	2.4(1.4-3.9)	7.0(5.2-9.3)	12.0(9.4-15.2)
17.8-25.9 ng/mL	4.8(2.4-9.3)	7.2(4.1-12.3)	17.9(12.7-24.9)	26.8(20.0-35.5)
> 25.9 ng/mL	2.6(0.6-9.9)	9.1(4.4-18.1)	23.6(15.0-36.0)	30.9(20.4-45.0)

Cardiovascular Mortality and Heart Failure-Related Hospitalization

Table 11. Hazard Ratios for Cardiovascular Mortality and Heart Failure-Related Hospitalization Events for HF Subjects in the Clinical Validation Study

	Hazard Ratio (95% CI, p value)		
Galectin-3 Category	≤ 17.8 ng/mL	17.8-25.9 ng/mL	> 25.9 ng/mL
Number of Subjects	647	170	78
Galectin-3*	1.0	1.51 (1.14-2.00, p= 0.004)	1.70 (1.19-2.42, p= 0.004)

**adjusted for baseline risk factors: age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes status, and smoking status.*

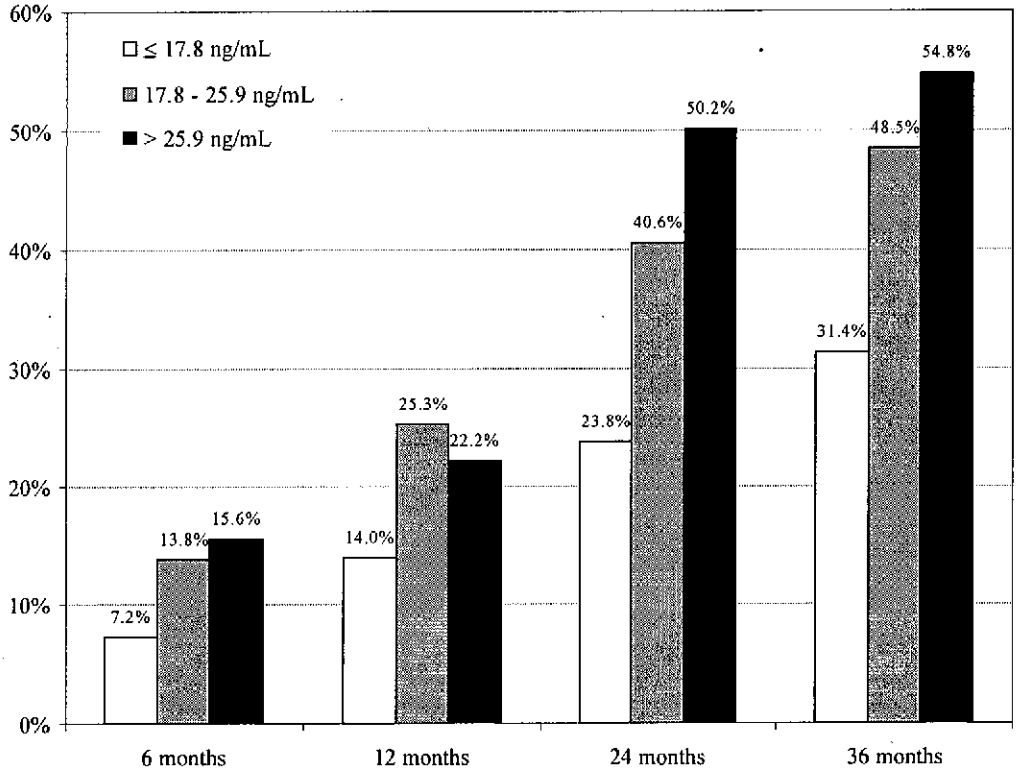

Figure 6: Cumulative Probability of Event for the Composite Endpoint of Cardiovascular Mortality and Heart Failure-Related Hospitalization, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

Table 12. Cumulative Probability (with 95% Confidence Intervals) of Event for Cardiovascular Mortality and Heart Failure-Related Hospitalization, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

	Cumulative Probability of Cardiovascular Mortality and Heart Failure-Related Hospitalization (95% CI) by Galectin-3 Category and Time Point (in percent)			
Galectin-3 Category	**6 months**	**12 months**	**24 months**	**36 months**
≤ 17.8 ng/mL	7.2% (5.4%-9.5%)	14.0 (11.5-17.0)	23.8 (20.6-27.4)	31.4 (27.6-35.6)
17.8-25.9 ng/mL	13.8 (9.4-20.1)	25.3 (19.4-32.7)	40.6 (33.4-48.7)	48.5 (40.5-57.2)
> 25.9 ng/mL	15.6 (9.2-25.8)	22.2 (14.4-33.2)	50.2 (38.9-62.8)	54.8 (42.9-67.6)

All-Cause Mortality

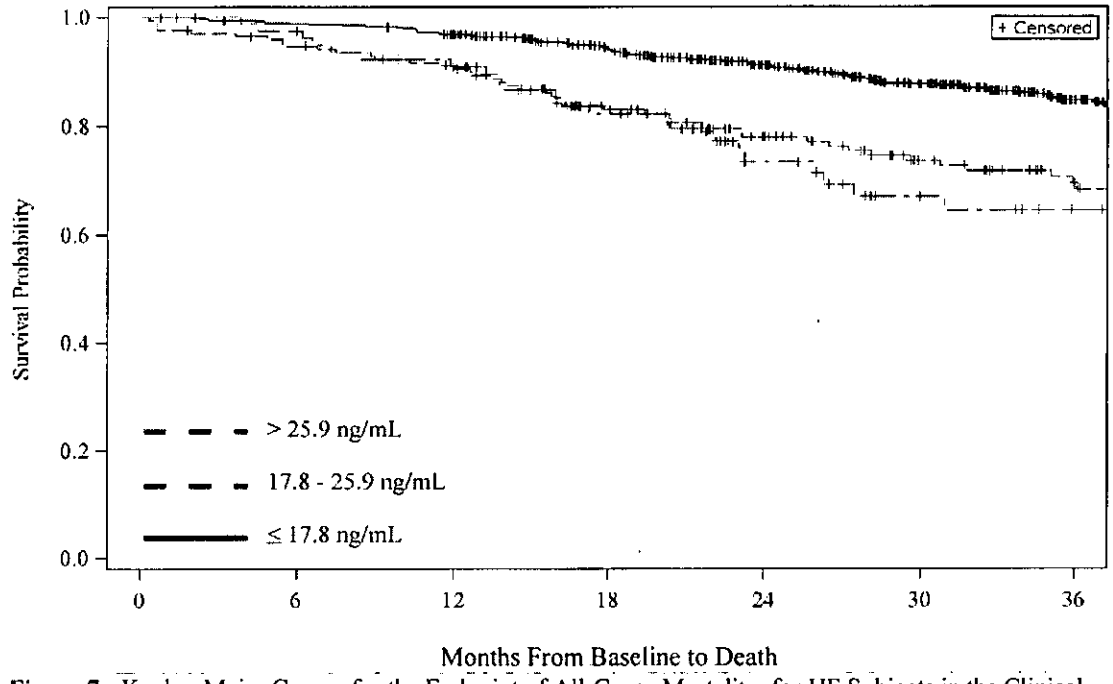

Figure 7: Kaplan-Meier Curves for the Endpoint of All-Cause Mortality, for HF Subjects in the Clinical Validation Study, by Baseline Galectin-3 Level

Table 13. Cumulative Probability (with 95% Confidence Intervals) of Event for the Endpoint of All-Cause Mortality, at Various Time Points and By Baseline Galectin-3 Level, for HF Subjects in the Clinical Validation Study

	Cumulative Probability of All-Cause Mortality Event (95% CI) by Galectin-3 Category and Time Point (in percent)			
Galectin-3 Category	**6 months**	**12 months**	**24 months**	**36 months**
≤ 17.8 ng/mL	1.2% (0.6%-2.5%)	3.3 (2.1-5.0)	8.7 (6.7-11.3)	15.3 (12.4-18.8)
17.8-25.9 ng/mL	5.3 (2.8-10.0)	8.9 (5.5-14.4)	22.0 (16.3-29.4)	30.5 (23.4-39.1)
> 25.9 ng/mL	2.6 (0.6-9.9)	9.1 (4.4-18.1)	26.6 (17.5-39.1)	35.5 (24.5-49.5)

Table 14. Hazard Ratios for All-Cause Mortality Events for HF Subjects in the Clinical Validation Study

	Hazard Ratio (95% CI, p value)		
Galectin-3 Category	≤ 17.8 ng/mL	17.8-25.9 ng/mL	> 25.9 ng/mL
Number of Subjects	647	170	78
Galectin-3*	1.0	1.84 (1.28-2.64, p= 0.001)	2.06 (1.31-3.23, p= 0.002)

**adjusted for baseline risk factors: age, gender, NYHA functional classification, left ventricular ejection fraction, diabetes status, and smoking status.*

Interpretation

The BGM Galectin-3 assay results should be interpreted in conjunction with clinical evaluation as an aid in the assessment of prognosis of patients diagnosed with chronic heart failure.

Patients with chronic heart failure with galectin-3 levels over 17.8 ng/mL were found to have a higher risk of adverse outcomes including mortality or hospitalization compared to patients with levels below 17.8 ng/mL. Galectin-3 levels between 17.8 ng/mL and 25.9 ng/mL should be interpreted with caution because these values lie within the reference range.

Interpretation Relative to Natriuretic Peptides

Galectin-3 and natriuretic peptides are measures of separate and distinct biological processes. Each marker provides independent and complementary information on the prognosis of patients with chronic heart failure.

Table 15 illustrates this for N-terminal pro B-type natriuretic peptide (NT-proBNP) in the clinical validation study by evaluating primary endpoint event rates by categories of galectin-3 and NT-proBNP.

Table 15. Event Rates at 6, 12, 24 and 36 Months for the Composite Endpoint of All-Cause Mortality and All-Cause Hospitalization, by Galectin-3 Category and NT-proBNP level, for HF Subjects in the Clinical Validation Study. The median value for NT-proBNP in the Clinical Validation Study was 848 pg/mL.

	Galectin-3 ≤ 17.8 ng/mL and NT-proBNP ≤ median	**Galectin-3 ≤ 17.8 ng/mL and NT-proBNP > median** *or* **Galectin-3 > 17.8 ng/mL and NT-proBNP ≤ median**	**Galectin-3 > 17.8 ng/mL and NT-proBNP > median**
Event rate at 6 months	19.4%	31.8%	42.7%
Event rate at 12 months	32.0%	50.0%	58.0%
Event rate at 24 months	55.3%	71.1%	85.7%
Event rate at 36 months	76.1%	85.8%	93.0%

Conclusion

Measurement of galectin-3 with the BGM Galectin-3 assay using a colorimetric microtiter plate reader is a safe and effective *in vitro* diagnostic device for use as an aid by clinicians in the assessment of prognosis of patients with chronic heart failure. Based on the foregoing, the performance of BGM Galectin-3 does not raise different questions of safety and effectiveness when used, as labeled, than those presented by the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, MD 20993

BG Medicine, Inc.
c/o Ms. Carol Adiletto
VP Clinical and Regulatory Affairs
610N Lincoln Street
Waltham, MA 02451

NOV 17 2010

Re: k093758
Trade Name: BGM Galectin-3
Regulation Number: 21 CFR §862.1117
Regulation Name: Test, Natriuretic Peptide
Regulatory Class: Class II
Product Code: OSX
Dated: November 3, 2010
Received: November 5, 2010

Dear Ms. Adiletto:

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. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Courtney Harper, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

BGMEDICINE

Indications for Use Statement

NOV 17 2010

510(k) Number (if known): K093758

Device Name: BGM Galectin-3™

Indications for Use:

BGM Galectin-3 is an *in vitro* diagnostic device that quantitatively measures galectin-3 in serum or EDTA-plasma by enzyme linked immunosorbant assay (ELISA) on a microtiter plate platform. BGM Galectin-3 is indicated for use in conjunction with clinical evaluation as an aid in assessing the prognosis of patients diagnosed with chronic heart failure (HF).

Prescription Use __X____ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Carol C. Benson

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety
510(k) K093758
