B-TYPE NATRIURETIC PEPTIDE/(BNP)

Intended Use

The i-STAT BNP test is an *in vitro* diagnostic test for the quantitative measurement of B-type natriuretic peptide (BNP) in whole blood or plasma samples using EDTA as the anticoagulant. BNP measurements can be used as an aid in the diagnosis and assessment of the severity of congestive heart failure.

Method Explanation

The i-STAT BNP test cartridge uses a two-site enzyme-linked immunosorbant assay (ELISA) method. Antibodies specific for BNP are located on an electrochemical sensor fabricated on a silicon chip. Also deposited in another location on the sensor silicon chip is an antibody/alkaline phosphatase enzyme conjugate specific to a separate portion of the BNP molecule. The whole blood or plasma sample is brought into contact with the sensors allowing the enzyme conjugate to dissolve into the sample. The BNP within the sample becomes labeled with alkaline phosphatase and is captured onto the surface of the electrochemical sensor during an incubation period of approximately seven minutes. The sample is washed off the sensors, as well as excess enzyme conjugate. Within the wash fluid is a substrate for the alkaline phosphatase enzyme. The enzyme bound to the antibody/antigen/antibody sandwich cleaves the substrate releasing an electrochemically detectable product. The electrochemical (amperometric) sensor measures this enzyme product which is proportional to the concentration of BNP within the sample.

Contents

Each i-STAT BNP cartridge provides a sample inlet, sensors to detect the BNP as described above, and all the necessary reagents needed to perform the test. The cartridge contains a buffer and preservatives. A list of reactive ingredients is indicated below:

Reactive Ingredient	Biological Source	Minimum Quantity
Antibody/Alkaline Phosphatase Conjugate	Murine IgG : Bovine Intestine	0.009 µg
IgG	Caprine IgG : Murine IgG	8.5 µg : 8 µg
Sodium Aminophenyl Phosphate	N/A	0.9 mg
Heparin	Porcine Intestine	0.45 IU
IgM	Murine IgM	0.3 µg

Metrological Traceability

The i-STAT System test for B-type natriuretic peptide (BNP) measures BNP amount-of-substance concentration in plasma or the plasma fraction of EDTA anticoagulated whole blood (units of measure: pg/mL or ng/L) for *in vitro* diagnostic use. BNP values assigned to i-STAT's controls and calibration verification materials are traceable to i-STAT's working calibrator prepared from synthetic BNP (Peptide International, Louisville, KY, Cat# 4212v). i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc.

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Reportable Range

The i-STAT BNP test will report 15 to 5000 pg/mL (ng/L). Samples below the reportable range will yield "<15 pg/mL" on the analyzer display screen. Samples above the reportable range will yield ">5000 pg/mL".

Reference Range

Whole blood and plasma samples from 165 apparently healthy donors were assayed. The upper 95% reference range was determined to be 50 pg/mL (ng/L).

Note: Each facility should establish its own reference range using the i-STAT BNP assay.

Clinical Significance

Congestive heart failure (CHF) is a complex clinical syndrome resulting in decreased cardiac output that is insufficient to meet the body's metabolic needs.[1] It may result from dysfunction of either ventricle in systole (contraction), diastole (relaxation) or both.[2] The most common underlying cause of CHF is coronary artery disease. Other causes include: hypertension, myocarditis, valvular heart disease and idiopathic (unknown).[3]

Common symptoms include: paroxysmal nocturnal dyspnea (PND), orthopnea, dyspnea on exertion (DOE), nocturnal cough and peripheral edema.[2] Clinical signs include elevated jugular venous pressure, rales on lung auscultation, the presence of a third heart sound and peripheral edema.[2] Unfortunately, these signs and symptoms are variable, and when present, non-specific as other clinical entities such as chronic obstructive pulmonary disease can produce a similar clinical picture.[4]

B-type natriuretic peptide (BNP) is one of a family of structurally similar peptide neurohormones that also includes atrial natriuretic peptide (ANP) and C-type natriuretic peptide (CNP) whose function is to regulate blood pressure, electrolyte balances, and fluid volume. ANP is stored in granules within the atria and released rapidly in response to atrial stretch. In contrast, BNP is synthesized, stored, and released primarily by the ventricular myocardium in response to volume expansion and pressure overload.[1] Pre-pro-BNP (134 amino acids) is synthesized in the cardiac myocytes and is processed to a pro-BNP (108 amino acids) precursor molecule. The pro-BNP is then subsequently cleaved into the physiologically active BNP (32 amino acids) and an N-terminal fragment referred to as N-Terminal pro-BNP (76 amino acids).[3]

Numerous clinical trials suggest the potential clinical usefulness of plasma BNP in:

1. the diagnosis of dyspnea and CHF[4,5]

2. the detection of left ventricular systolic and diastolic dysfunction[6,7]

3. the prognosis of patients with CHF and acute coronary syndromes[8,9] and

4. therapy monitoring for CHF patients[10,11]

Multiple studies establish the value of BNP for facilitating the diagnosis of CHF in patients presenting with dyspnea.[12] Davis et al. measured levels of ANP and BNP in 52 patients presenting with acute dyspnea.[12,13] They found that admission plasma BNP concentrations more accurately reflected the final diagnosis than did ejection fraction (EF) levels or ANP plasma concentrations. Morrison et al. also showed that rapid testing of BNP could help differentiate pulmonary from cardiac etiologies of dyspnea.[4] Furthermore, the Task Force of the European Society of Cardiology for the Diagnosis and Treatment of Chronic HF has included the use of natriuretic peptide (e.g., BNP) testing along with electrocardiography and chest x-rays in their guidelines for the diagnosis or rule out of HF.[14]

The Breathing Not Properly study, a 1586 patient multinational prospective study, validated the clinical utility of rapid measurement of BNP, used in conjunction with other clinical information, for the diagnosis or exclusion of CHF in the emergency department.[15] BNP levels were much higher in patients with subsequent CHF than in those with non-cardiac dyspnea (675 pg/mL vs 110 pg/mL). A BNP cutoff value of 110 pg/mL had a sensitivity of 90% and a specificity of 76% for differentiating CHF from other causes of dyspnea,

and a cutoff value of 50 pg/mL had a negative predicative value of 96%. There was a 43% indecision rate among physicians in the ED trying to make a diagnosis in patients with dyspnea. Had BNP levels been available to those physicians, the indecision rate would have been reduced to 11%. In multivariate analysis, BNP levels always contributed to the diagnosis, even after consideration of the history and physical exam.

BNP levels are also raised in patients with left ventricular dysfunction, and the values can be used to assess the severity of CHF, as they correlate with both New York Heart Association (NYHA) functional class and patient prognosis.[16]

Steg et al. indicated in 2005 that BNP measurement is consistently superior to a single echocardiographic determination of left ventricular EF in identifying patients with CHF, regardless of the threshold value.[16] Two-dimensional echocardiography was less sensitive than a single determination of BNP in diagnosing CHF. However, the two variables have marked additive diagnostic value and when combined have a much improved accuracy compared to either method alone. This strongly suggests that, where applicable, they should be used together.[16]

Studies also indicate that BNP also has a burgeoning role in the prognostic assessment of patients with heart failure.[17] BNP is a powerful prognostic indicator for patients with CHF at all stages of the disease and seems to be a better predictor of survival than many traditional prognostic indicators, such as New York Heart Association class, serum creatinine values, and possibly left ventricular ejection fraction.[18] The relative risk of death increases by about 35% for each 100 pg/mL increase in BNP in patients with CHF.[18] Raised BNP values also predict the survival in patients not known to have CHF, with the risk doubled in patients with a BNP value >20 pg/mL.[18]

BNP has also been shown to predict morbidity and mortality in other cardiovascular conditions, such as acute coronary syndromes and acute myocardial infarction.[19] ACS patients with increased BNP levels have a higher rate of cardiac complications and higher mortality post myocardical infarction.

When a panel of neurohormones (including BNP and catecholemines) was measured one to four days after acute infarction, BNP was the only independent predictor of left ventricular ejection fraction (LVEF <40%) and was the most powerful predictor of death within four months after infarction.[20] In 2,525 AMI patients, the magnitude of BNP elevation correlated with mortality, heart failure, and recurrent infarction at both 30 days and 10 months.[8] A strategy of combining EF and BNP improved risk stratification beyond using either alone.[21]

EXPECTED VALUES
Non-heart Failure Population

Plasma samples from 890 individuals (465 females, 425 males) who had not been diagnosed with heart failure were tested with the AxSYM® BNP assay. This population included non-hospitalized patients with renal disease (not on dialysis), diabetes, hypertension and chronic obstructive pulmonary disease. BNP levels for the patients with renal disease, diabetes, hypertension and chronic obstructive pulmonary disease were not statistically different from the population of apparently healthy individuals. The data from this study are summarized in the following table.*

Non-Heart Failure Population - All (Age Group)

	All	<45 Years	45-54 Years	55-64 Years	65-74 Years	75+ Years
Sample Size (N=)	890	205	146	171	248	120
Median (pg/mL)	21	17	9	24	23	31
Mean (pg/mL)	39	28	21	37	47	63
SD (pg/mL)	66	36	30	48	80	109
95th Percentile	135	85	87	119	160	254
Percentage < 100 pg/mL	91.5%	96.6%	95.2%	94.2%	87.1%	83.3%
Minimum (pg/mL)	0	0	0	0	0	0
Maximum (pg/mL)	907	263	142	380	907	837

Non-Heart Failure Population - Males (Age Group)

	All	<45 Years	45-54 Years	55-64 Years	65-74 Years	75+ Years
Sample Size (N=)	425	107	71	94	115	38
Median (pg/mL)	14	12	1	17	21	37
Mean (pg/mL)	30	23	9	26	47	49
SD (pg/mL)	61	34	14	45	96	51
95th Percentile	104	73	40	80	150	121
Percentage < 100 pg/mL	94.8%	97.2%	100.0%	97.9%	88.7%	89.5%
Minimum (pg/mL)	0	0	0	0	0	0
Maximum (pg/mL)	907	200	57	380	907	254

Non-Heart Failure Population - Females (Age Group)

	All	<45 Years	45-54 Years	55-64 Years	65-74 Years	75+ Years
Sample Size (N=)	465	98	75	77	133	82
Median (pg/mL)	26	23	23	37	23	25
Mean (pg/mL)	46	34	34	51	46	69
SD (pg/mL)	70	37	36	48	63	126
95th Percentile	150	89	111	155	159	266
Percentage < 100 pg/mL	88.4%	95.9%	90.7%	89.6%	85.7%	80.5%
Minimum (pg/mL)	0	0	0	0	0	0
Maximum (pg/mL)	837	263	142	230	374	837

* Representative data, results in individual laboratories may vary from these data.

Due to demographic population differences, the reference range should be established at each laboratory.

Heart Failure Population

Plasma samples from 693 patients with diagnosed heart failure (231 females, 462 males) were tested with the AxSYM BNP assay. All patients in this population were categorized according to the functional classification system published by the New York Heart Association (NYHA).[22] This system divides heart failure patients into one of four categories of increasing disease progression (classes I to IV) based upon a subjective assessment of the patient's clinical signs and symptoms. The data from this study are summarized in the following table.*

Heart Failure Population - All					
	NYHA Functional Class				
	All	**I**	**II**	**III**	**IV**
Sample Size (N=)	693	124	319	190	60
Median (pg/mL)	298	133	266	335	1531
Mean (pg/mL)	578	320	432	656	1635
SD (pg/mL)	771	388	574	841	1097
5th Percentile	14	9	15	12	188
95th Percentile	2154	1257	1534	2516	>4000
Percentage ≥ 100 pg/mL	74.2%	58.1%	73.0%	79.0%	98.3%
Minimum (pg/mL)	0	3	0	0	14
Maximum (pg/mL)	>4000	1651	>4000	>4000	>4000

Heart Failure Population - Males					
	NYHA Functional Class				
	All	**I**	**II**	**III**	**IV**
Sample Size (N=)	462	94	215	121	32
Median (pg/mL)	268	122	258	293	1645
Mean (pg/mL)	524	314	409	597	1646
SD (pg/mL)	719	390	539	821	1032
5th Percentile	12	9	14	22	265
95th Percentile	1976	1281	1356	2288	3654
Percentage ≥ 100 pg/mL	71.0%	56.4%	70.7%	76.0%	96.9%
Minimum (pg/mL)	0	3	0	0	14
Maximum (pg/mL)	>4000	1408	3782	>4000	>4000

| Heart Failure Population - Females					
			NYHA Functional Class		
	All	**I**	**II**	**III**	**IV**
Sample Size (N=)	231	30	104	69	28
Median (pg/mL)	385	174	298	466	1408
Mean (pg/mL)	685	341	481	760	1623
SD (pg/mL)	858	388	641	870	1186
5th Percentile	16	14	21	12	244
95th Percentile	2593	1022	2031	2718	>4000
Percentage ≥ 100 pg/mL	80.5%	63.3%	77.9%	84.1%	100.0%
Minimum (pg/mL)	0	10	0	0	173
Maximum (pg/mL)	>4000	1651	>4000	>4000	>4000

* Representative data, results in individual laboratories may vary from these data.

A box and whiskers plot of the clinical study population, broken down by NYHA classification, is presented in the following graph. The dashed line represents 100 pg/mL, the suggested decision threshold for the AxSYM BNP assay. In support of previous literature reports,[23] these data show a progressive increase in BNP concentrations with increases in NYHA classifications. This analysis indicates that BNP measurements provide objective information for use in the assessment of the severity of heart failure.
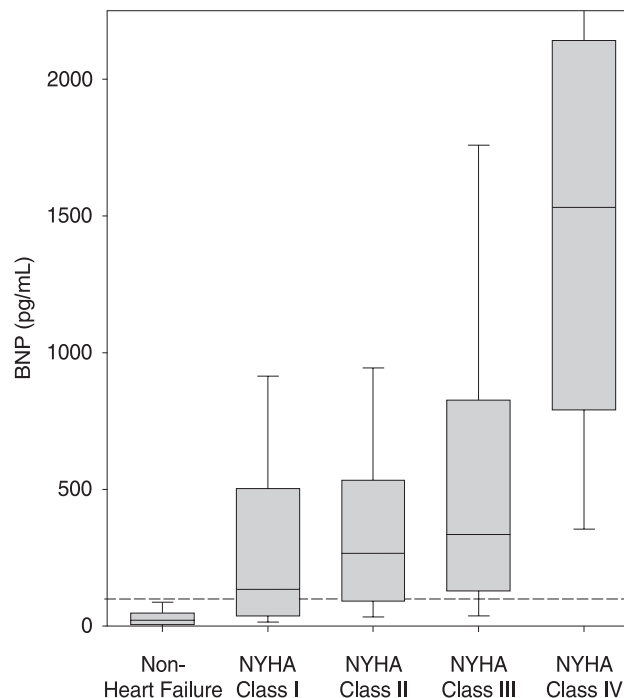
Data from the above clinical study were used to generate the Receiver Operating Characteristic (ROC) curve of BNP decision thresholds versus clinical sensitivity and clinical specificity as shown in the following graph. At a decision threshold of 100 pg/mL, the BNP assay demonstrated a clinical sensitivity and specificity of 74.2% and 91.5%, respectively, in this study. The area under the curve (AUC) is 0.90 (0.86 to 0.92, 95% CI).

BNP ROC Curve
Heart Failure Population (n=693) and
Non-Heart Failure Population (n=890)
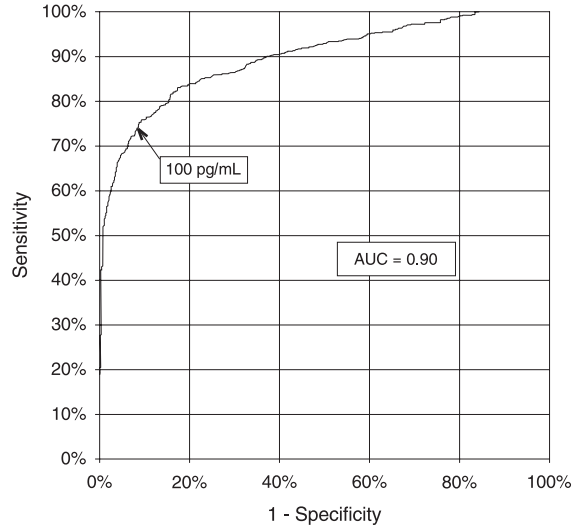
The i-STAT BNP Calibrators are traceable to an internal reference standard that has been prepared gravimetrically with synthetic BNP. The internal reference standard underwent a one-time value assignment to align with the ARCHITECT BNP assay with a decision threshold of 100 pg/mL.

An age-matched analysis of the heart failure and non-heart failure populations was performed based on the data published by the American Heart Association in the 2000 Heart and Stroke Statistical Update[24] and according to the age structure of the United States population.[25] The age distributions in the intended use population are approximately as follows: individuals less than 45 years old comprise 9%, individuals 45-54 years old comprise 11%, individuals 55-64 years old comprise 22%, individuals 65-74 years old comprise 26%, and individuals 75 years and older comprise 32%. The resulting combined AUC is 0.87 (0.85 to 0.90, 95% CI).

The clinical sensitivity and specificity using a decision threshold of 100 pg/mL is presented in the following table.*

Males (Age Group)						
	All	**<45 Years**	**45-54 Years**	**55-64 Years**	**65-74 Years**	**75+ Years**
Sensitivity	71.0% (328/462)	47.1% (8/17)	57.1% (24/42)	57.3% (51/89)	70.6% (115/163)	86.1% (130/151)
95% Confidence Interval	66.6 to 75.1%	23.0 to 72.2%	41.0 to 72.3%	46.4 to 67.7%	62.9 to 77.4%	79.5 to 91.2%
Specificity	94.8% (403/425)	97.2% (104/107)	100.0% (71/71)	97.9% (92/94)	88.7% (102/115)	89.5% (34/38)
95% Confidence Interval	92.3 to 96.7%	92.0 to 99.4%	94.9 to 100.0%	92.5 to 99.7%	81.5 to 93.8%	75.2 to 97.1%

Females (Age Group)						
	All	**<45 Years**	**45-54 Years**	**55-64 Years**	**65-74 Years**	**75+ Years**
Sensitivity	80.5% (186/231)	44.4% (4/9)	73.3% (11/15)	50.0% (13/26)	80.6% (58/72)	91.7% (100/109)
95% Confidence Interval	74.8 to 85.4%	13.7 to 78.8%	44.9 to 92.2%	29.9 to 70.1%	69.5 to 88.9%	84.9 to 96.2%
Specificity	88.4% (411/465)	95.9% (94/98)	90.7% (68/75)	89.6% (69.77)	85.7% (114/133)	80.5% (66/82)
95% Confidence Interval	85.1 to 91.2%	89.9 to 98.9%	81.7 to 96.2%	80.6 to 95.4%	78.6 to 91.2%	70.3 to 88.4%

* Representative data, results in individual laboratories may vary from these data.

Performance Characteristics

Precision data were collected as follows: Duplicates of each control were tested daily for a period of 20 days for each of 3 lots of cartridges, resulting in a total of 434 replicates. The average statistics are presented below.

Whole blood imprecision data were collected as follows: whole blood samples from 5 healthy donors were spiked to low, intermediate and high BNP concentrations affording 15 samples, each of which was measured in 10 i-STAT BNP cartridges from a single cartridge lot; three lots of cartridges were employed. The mean within-sample BNP concentration ranged from 84 – 3925 pg/mL and the within-sample imprecision (%CV) ranged from 3.4 to 9.4%; the average BNP concentration and imprecision were 1464 pg/mL and 6.5%, respectively.

Method comparison data were collected using CLSI guideline EP9-A2.[26] Venous blood samples were collected in EDTA evacuated tubes and analyzed in duplicate on the i-STAT System. A portion of the specimen was centrifuged and the separated plasma was analyzed in duplicate on the i-STAT System and on the comparative method within 1 hour of collection. Deming regression analysis[27] was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the first data set, Sxx and Syy refer to estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively. Sy.x is the standard error of the estimate, and r is the correlation coefficient.* Method comparisons may vary from site to site due to differences in sample handling, comparative method calibration and other site specific variables.

The i-STAT BNP assay is designed for quantitation of BNP in whole blood or plasma samples. A series of samples for comparison of whole blood and plasma results was prepared from blood drawn from 25 nominally healthy donors. For each donor, whole blood (unspiked) and plasma obtained via centrifugation were first run simultaneously in duplicate i-STAT BNP test cartridges. A whole blood sample was then spiked with BNP and, following a short equilibration period, a plasma sample was prepared by centrifugation and the whole blood and plasma samples were run simultaneously in duplicate. Three lots of i-STAT BNP test cartridges were employed with a single lot being used for each donor. The results of Deming regression of whole blood vs plasma (x-axis) correlation data are summarized below for all samples ([BNP] < 5000 pg/mL) and separately for samples with [BNP] < 1000 pg/mL.

*The usual warning relating to the use of regression analysis is summarized here as a reminder. For any analyte, "if the data is a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from estimates may be invalid".[26] The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method range in overcoming the problem. As a guide, the range of data can be considered adequate if r>0.975.

Precision Data (pg/mL)

Aqueous Control	Mean	%CV (within-run)	%CV (total)
Level 1	126	9.0	11.1
Level 2	1551	6.6	8.1
Level 3	3337	8.0	9.8

Method Comparison

	Abbott ARCHITECT
N	433
Mean (pg/mL)	482.1
Sxx (pg/mL)	38.1
Syy (pg/mL)	97.6
Slope	0.971
Intercept	-14.4
Sy.x	198.0
Xmin	5
Xmax	4797.7
Correlation, r	0.972

Equivalence of Whole Blood and Plasma (x-axis)

	Plasma([BNP]<5000pg/mL)	Plasma([BNP]<1000pg/mL)
N	49	36
Mean (pg/mL)	776	146
Sxx (pg/mL)	122.0	18.5
Syy (pg/mL)	98.1	16.5
Slope	0.946	1.01
Intercept	50.2	-0.2
Sy.x	107.3	28.3
Xmin	0	0
Xmax	4173	922
Correlation,r	0.997	0.996

Analytical Sensitivity

The limit of blank (commonly termed analytical sensitivity) was estimated at 14 pg/mL by calculating two times the total imprecision determined using a BNP-depleted plasma material (measured to be <5 pg/mL BNP) over a 20-day imprecision study using three separate lots of BNP cartridges and six i-STAT 1 analyzers.

Analytical Specificity

The BNP method is specific for the B-type natriuretic peptide. The following muscle proteins were tested at both 1000 pg/mL and 20000 pg/mL concentrations and found to have no detectable crossreactivity for BNP: ANP, CNP, and N-terminal pro-BNP.

Recovery

The dilution linearity of the i-STAT BNP test was investigated using EDTA whole blood and plasma samples derived from three separate donors. For each donor, the original BNP negative sample and a BNP spiked sample were prepared. This process yielded three BNP positive whole blood samples that were then assayed in duplicate for each of three separate i-STAT BNP cartridge lots. These whole blood samples were then diluted using an equal mass of the original unspiked whole blood and assayed in duplicate. From this whole blood data, the BNP recovery was calculated.

Whole Blood Sample	Concentration (pg/mL)	Diluted Concentration (pg/mL)	% Recovery
A	590	312	106%
B	2765	1429	103%
C	5123	2803	109%

The plasma derived from these three donors was combined in all pairwise combinations in equal volumes. These combinations were then assayed in duplicate for each of three separate i-STAT BNP cartridge lots. The BNP recovery for each pair was calculated using the average of the six results.

Plasma Blood Sample	Concentration pg/mL)	Diluted Concentration (pg/mL)	% Recovery
A	590	—	—
B	2764	—	—
C	5123	—	—
A+B	—	1570	94%
B+C	—	3992	101%
A+C	—	2734	96%

A plasma sample was spiked with BNP to a value of approximately 5000 pg/mL and the concentration was determined by duplicate measurements with i-STAT BNP test cartridges; the result was found to be within 200 pg/mL of the intended target. This sample was subjected to a series of dilutions with fresh, unspiked plasma in order to prepare a range of concentrations. The concentration of each sample/dilution was calculated based on the measured concentration of the initial solution and the dilutions performed. The diluted samples were then measured in i-STAT BNP test cartridges (N = 6-10). The procedure was repeated with a whole blood sample. The results of these experiments are summarized in the following table.

Sample	Dilution	Calculated [BNP] (pg/mL)	Measured [BNP] (pg/mL)	%Recovery
Plasma	1	52	57	110%
Plasma	2	104	114	110%
Plasma	3	259	265	103%
Plasma	4	518	560	108%
Plasma	5	1036	1002	97%
Plasma	6	2072	2277	110%
Plasma	7	3107	3384	109%
Plasma	8	4143	4222	102%
Whole Blood	1	44	41	93%
Whole Blood	2	88	88	100%
Whole Blood	3	269	287	107%
Whole Blood	4	537	554	103%
Whole Blood	5	725	720	99%
Whole Blood	6	1450	1367	94%
Whole Blood	7	3042	2826	93%
Whole Blood	8	4056	3856	95%

Test Limitations

The frequency of suppressed results is affected by atmospheric pressure. Suppressed result rates may increase with higher elevations (decreased barometric pressure) and may become persistent if testing is performed at more than 7500 feet above sea level. Where unavailability of results is unacceptable, Abbott Point of Care recommends having an alternate test method available.

Samples from patients who have been exposed to animals or who have received therapeutic or diagnostic procedures employing immunoglobulins or reagents derived from immunoglobulins may contain antibodies, e.g., HAMA or other heterophile antibodies, which may interfere with immunoassays and produce erroneous results.[28-34] The generation of potentially interfering antibodies in response to bacterial infections has been reported.[28] While this product contains reagents that minimize the effect of these interferents and QC algorithms designed to detect their effects, the possibility of interference causing erroneous results should be evaluated carefully in cases where there are inconsistencies in the clinical information.

Partially clotted samples can result in elevated BNP readings above the reference range, as well as quality check codes. To prevent this from occurring, upon drawing the whole blood sample into an EDTA collection tube, the sample should be inverted gently at least 10 times to ensure even dissolution of the anticoagulant.

Grossly hemolyzed samples can cause a decreased alkaline phosphatase activity, resulting in decreased detection of BNP, increased assay backgrounds, and/or quality check codes.

Hematocrits in the range of 0-60% PCV have been demonstrated not to affect results. Samples with hematocrit levels above this range have demonstrated increases in the test imprecision and quality check codes.

The analyzer must remain on a flat surface with the display facing up during testing. Motion of the analyzer during testing can increase the frequency of suppressed results or quality check codes. A level surface includes running the handheld in the downloader/recharger.

Measurements of BNP should occur prior to nesiritide (Natrecor) recombinant BNP treatment, or 2 hours post-treatment.[35]

Interference Testing

The following substances were found to have no significant effect (less than 10%) on the BNP method, when added to a plasma pool containing approximately 1000 pg/mL of B-type natriuretic peptide at the concentrations indicated:

Interference studies were based on CLSI guideline EP7-A.[36]

Compound	Test Level (µmol/L unless otherwise indicated)
Acetaminophen	1660
Allopurinol	294
Ampicillin	152
Ascorbic Acid	227
Acetyl Salicylic Acid	3330
Atenolol	37.6
Caffeine	308
Captopril	23
Chloramphenicol	155
Diclofenac	169
Digoxin	6.15
Dopamine	5.87
Enalaprilat	0.86
Erythromycin	81.6
Furosemide	181
Sodium Heparin	90 U/mL
Ibuprofen	2425
Isosorbide dinitrate	636
Methyldopa	71
Nicotine	6.2
Nifedipine	1156
Phenytoin	198
Propranolol	7.71
Salicylic Acid	4340
Theophylline	222
Verapamil	4.4
Warfarin	64.9

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