Intended Use

The Alere Triage® BNP test is intended for use with the Beckman Coulter Access Family of Immunoassay Systems for the In Vitro quantitative measurement of B-type natriuretic peptide (BNP) in plasma specimens using EDTA as the anticoagulant. The test is intended to be used for the following indications:

- as an aid in the diagnosis of congestive heart failure (also referred to as heart failure)
- as an aid in the assessment of severity of congestive heart failure
- for the risk stratification of patients with acute coronary syndromes
- for the risk stratification of patients with heart failure

Summary and Explanation

It is estimated that 5.8 million people in the United States have heart failure with approximately 670,000 new cases occurring each year. Congestive heart failure (CHF) occurs when the heart cannot deliver a sufficient amount of blood to the body. This condition can occur at any age but is most prevalent in an aged population. Symptoms of CHF include shortness of breath, fluid retention and respiratory distress. These symptoms are often vague and nonspecific for detecting early stages of CHF.

B-type natriuretic peptide (BNP) is a member of a class of hormones that regulate blood pressure. The heart is the main source of circulating BNP in humans. The molecule is released into the blood in response to increased heart pressure. Various studies have demonstrated that increased levels of circulating BNP are found in early stages of CHF. The level of BNP in the blood continues to increase as the CHF disease advances. The Alere Triage® BNP test offers an objective, noninvasive measurement for assessing patients for CHF and risk stratification in patients with acute coronary syndromes (ACS).

Principles of the Procedure

The Alere Triage® BNP test is a two-site immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel with mouse monoclonal anti-human BNP antibody-alkaline phosphatase conjugate and paramagnetic particles coated with mouse Omniclonal anti-human BNP antibody. BNP in human plasma binds to the immobilized anti-BNP on the solid phase, while the mouse anti-BNP conjugate reacts specifically with bound BNP. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A chemiluminescent substrate, Lumi-Phos® 530, is added to the reaction vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of BNP in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

Product Information

Alere Triage® BNP Reagent Pack

Cat. No. 98200: 100 determinations, 2 packs, 50 tests/pack

- Provided ready to use.
- Store upright and refrigerate at 2-10 °C.
- Refrigerate at 2-10 °C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2-10 °C.
- Stable at 2-10 °C for 28 days after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e., broken elastomer), discard the pack.
- All antisera are polyclonal unless otherwise indicated.

<table>
<thead>
<tr>
<th>R1a</th>
<th>Paramagnetic particles coated with mouse Omniclonal anti-human BNP antibody suspended in TRIS buffered saline, with bovine serum albumin (BSA), 0.1% ProClin® 300, and &lt; 0.1% sodium azide.</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1b</td>
<td>Purified mouse and goat IgG in TRIS buffered saline, with bovine serum albumin (BSA), 0.1% ProClin 300 and &lt; 0.1% sodium azide.</td>
</tr>
<tr>
<td>R1c</td>
<td>Mouse monoclonal anti-human BNP antibody-alkaline phosphatase bovine conjugate in PBS buffered saline with BSA, 0.1% ProClin 300, and &lt; 0.1% sodium azide.</td>
</tr>
</tbody>
</table>

Warnings and Precautions

- For In Vitro Diagnostic Use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local, state and federal regulations and guidelines.
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.
- The Alere Triage® BNP test should not be used as absolute evidence for CHF. The results should be interpreted along with clinical findings and other laboratory test results.
- Blood concentrations of BNP may be elevated in patients who are experiencing a heart attack, patients that are candidates for renal dialysis, and patients that have had renal dialysis.
GHS Hazard Classification

GXM/MXLH PMP WARNING

H317 May cause an allergic skin reaction.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray
P272 Contaminated work clothing should not be allowed out of the workplace
P280 Wear protective gloves/protective clothing/eye protection/face protection
P302+P352 IF ON SKIN: Wash with plenty of soap and water
P321 Specific treatment (see First aid measures on this label)
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P362+P364 Take off contaminated clothing and wash it before reuse
P501 Dispose of contents/container to [X]

European Hazard Classification

GXM/MXLH PMP WARNING

Xi;R43 May cause sensitization by skin contact.
R43 After contact with skin, wash immediately with plenty of soap and water.
S28 Wear suitable gloves.
S37

- The Safety Data Sheet (SDS) is available upon request.

Specimen Collection and Preparation

Plasma (EDTA) is the required sample. Use of plastic blood draw tubes containing K2 EDTA as an anticoagulant for sample collection permits an accurate measurement of plasma BNP concentrations for sample collection (Davidson et al., Circulation 91: 1276, 1995). Other specimen types have not been evaluated.

Observe the following recommendations for handling, processing, and storing blood samples 10:

- Collect all blood samples observing routine precautions for venipuncture.
- Mix the blood specimen by gently inverting the tube several times.
- Keep tubes stoppered at all times.
- Samples should be tested as soon as possible after collection. However, if it is not possible to test the samples immediately, the following is recommended:
  - Blood and plasma specimens may be stored at room temperature (or chilled) for testing within 7 hours of collection.
  - Plasma specimens may be stored chilled for testing within 24 hours of collection.
  - Transport specimens at room temperature or chilled and avoid extreme temperatures.
- For longer storage, transfer at least 500 μL of cell-free sample to a storage tube. Tightly stopper the tube immediately and freeze at -20 °C or colder in a non-defrosting freezer. When thawing, allow samples to equilibrate to room temperature for a minimum of 30 minutes prior to testing.
- Thaw samples only once.
- It is recommended to avoid using severely hemolyzed specimens whenever possible. If a specimen appears to be severely hemolyzed, another specimen should be obtained and tested.

Use the following guidelines when preparing specimens, unless instructed otherwise in the product insert:

- Ensure residual fibrin and cellular matter has been removed prior to analysis.
- Follow blood collection tube manufacturer's recommendations for centrifugation.

Each laboratory should determine the acceptability of its own blood collection tubes. Variations in these products may exist between manufacturers and, at times, from lot to lot.

Materials Provided

R1 Alere Triage® BNP Reagent Packs

Materials Required but Not Provided

1. Alere Triage® BNP Calibrators
   Provided at zero, and approximately 25, 100, 500, 2500, and 5000 pg/mL.
   Cat. No. 98202

2. Alere Triage® BNP QC Controls.
   Provided at approximately 80, 400, and 2200 pg/mL.
   Cat. No. 98201

3. Access*** Substrate
   Cat. No. 81906

4. Access Wash Buffer II
   NOTE: The required wash buffer II catalog number is dependent upon your current instrument status. Please contact Beckman Coulter technical support if you are unsure of which buffer to order.
   Cat. No. A16792 (Access®, Access® 2, SYNCHRON® LXi, UniCel® DxC600i)
   Cat. No. A16793 (UniCel DxC 660i, UniCel DxC 680i, UniCel DxC 860i, UniCel DxC 880i, UniCel Dxl 600, UniCel Dxl 800)
5. One of the following immunoassay systems:
   Access, Access 2, Synchron LXI 725, UniCel DxC 660i, UniCel DxC 680i, UniCel DxC 860i, UniCel DxC 880i, UniCel Dxl 600, UniCel Dxl 800 or UniCel DxC600i

**Procedural Comments**

1. Refer to the appropriate system manuals and/or help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
3. Use 55 μL of sample for each determination in addition to the sample container and system dead volumes. Use one hundred fifty-five (155) μL of sample in addition to the sample container and system dead volumes for each determination run with the Dxl system onboard dilution feature. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
4. The unit of measure for sample results is pg/mL.

**Procedure**

Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

**Calibration Details**

An active calibration curve is required for all tests. For the Alere Triage® BNP test, calibration is required every 28 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

**Quality Control**

Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period 

1. Include Alere Triage® BNP QC Controls for the Beckman Coulter® Access Family of Immunoassay Systems that cover at least two levels of the analyte. The use of non-Alere Control materials is not recommended. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer’s instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

**Results**

Patient test results are determined automatically by the system software using a smoothing spline math model. The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Patient test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

**Interpretation of the Results**

The Beckman Coulter Access Family of Immunoassay Systems calculates the test results automatically. A number in pg/mL represents the amount of BNP present in the sample.

- BNP results less than or equal to 100 pg/mL are representative of normal values in patients without CHF.
- BNP results greater than 100 pg/mL are considered abnormal and suggestive of patients with CHF.
- BNP results of > 5000 pg/mL are considered very high values for BNP and exceed the upper limits of the BNP test.
- Higher BNP concentrations measured in the first 72 hours after an acute coronary syndrome are associated with an increased risk of death, myocardial infarction, and CHF.
- Higher BNP concentrations or the lack of a decrease in the BNP concentration from hospital admission to discharge indicate an increased risk of hospitalization or death in patients with heart failure.

**Limitations of the Procedure**

The results of the Alere Triage® BNP test should be evaluated with all clinical and laboratory data available. If Alere Triage® BNP test results do not agree with the clinical evaluation, additional tests should be performed.

This test has been evaluated with plasma using EDTA as the anticoagulant. Serum and blood or plasma specimens obtained using other anticoagulants (e.g., heparin or citrate) have not been evaluated and should not be used.

Other factors may interfere with the Alere Triage® BNP test and may cause erroneous results. These include technical or procedural errors, as well as additional substances in blood specimens that are not listed or exceed the concentrations listed in the Interfering Substances and the Analytical Specificity sections.

1. Samples can be accurately measured within the analytic range of the lower limit of detection and the highest calibrator value [approximately 1–5000 pg/mL]. When the Dxl system onboard dilution feature is used, the system will report results approximately 4250-10,000 pg/mL. If a sample contains more than the stated value of the highest Alere Triage® BNP Calibrator (SS), report the result as greater than that value [i.e. > 5000 pg/mL]. Alternatively, dilute one volume of sample with one volume of Access Wash Buffer. Refer to the appropriate system manuals and/or Help system for instructions on entering a sample dilution in a test request. The system reports the results adjusted for the dilution. The Dxl system onboard dilution feature automates the dilution process, using one volume of sample with one volume of UniCel Dxl Access Immunoassay Systems Wash Buffer II, allowing samples to be quantitated up to approximately 10,000 pg/mL. The system reports the results adjusted for the dilution.

2. Human anti-mouse antibodies (HAMA) may be present in samples from patients who have received immunotherapy utilizing monoclonal antibodies. Additionally, other heterophile antibodies such as human anti-goat antibodies, may be present in patient samples. This test has been specifically formulated to minimize the effects of these antibodies on the assay. However, carefully evaluate results from patients suspected of having such antibodies.

3. The Alere Triage® BNP test does not demonstrate any “hook” effect when tested up to BNP concentrations of 150,000 pg/mL.

4. The Alere Triage® BNP test results should be interpreted in light of the total clinical presentation of the patient, including: clinical history, data from additional tests and other appropriate information.


Specific Performance Characteristics

Performance characteristics were determined using the Access immunoassay platform.

Methods Comparison

A comparison of 412 EDTA plasma samples measured values using the Alere Triage® BNP test on the Access Immunoassay System and the Alere Triage® BNP test gave the following statistical data using Passing-Bablok regression analysis:

<table>
<thead>
<tr>
<th>n</th>
<th>Range of Observations (pg/mL)</th>
<th>Intercept (pg/mL)</th>
<th>Slope</th>
<th>Correlation Coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>412</td>
<td>5–4970</td>
<td>-0.15</td>
<td>1.00</td>
<td>0.950</td>
</tr>
</tbody>
</table>

The results indicate that Alere Triage® BNP test results can be used interchangeably.

Dilution Recovery (Linearity)

Multiple dilutions of 4 plasma samples spiked with purified BNP to final concentrations of approximately 5000 pg/mL using unspiked plasma as the diluent resulted in the following data:

<table>
<thead>
<tr>
<th>Percent Recovery</th>
<th>Donor 1</th>
<th>Donor 2</th>
<th>Donor 3</th>
<th>Donor 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>102.2%</td>
<td>103.4%</td>
<td>106.0%</td>
<td>100.3%</td>
</tr>
<tr>
<td>Level 2</td>
<td>101.1%</td>
<td>101.5%</td>
<td>97.1%</td>
<td>98.4%</td>
</tr>
<tr>
<td>Level 3</td>
<td>97.0%</td>
<td>98.7%</td>
<td>94.8%</td>
<td>96.1%</td>
</tr>
<tr>
<td>Level 4</td>
<td>93.3%</td>
<td>93.3%</td>
<td>90.1%</td>
<td>91.5%</td>
</tr>
<tr>
<td>Level 5</td>
<td>89.9%</td>
<td>92.2%</td>
<td>88.0%</td>
<td>88.2%</td>
</tr>
<tr>
<td>Level 6</td>
<td>92.1%</td>
<td>91.2%</td>
<td>83.3%</td>
<td>89.5%</td>
</tr>
<tr>
<td>Level 7</td>
<td>91.6%</td>
<td>90.6%</td>
<td>87.8%</td>
<td>90.0%</td>
</tr>
<tr>
<td>Level 8</td>
<td>91.0%</td>
<td>88.2%</td>
<td>87.9%</td>
<td>87.9%</td>
</tr>
<tr>
<td>Level 9</td>
<td>88.1%</td>
<td>89.4%</td>
<td>86.6%</td>
<td>85.0%</td>
</tr>
</tbody>
</table>

Imprecision

Reproducibility of the Alere Triage® BNP test was determined in a study using commercially available and in-house human control material with two lots of reagents. The study included a total of 20 assays, 2 replicates per assay, over 20 days. Representative data were calculated based on NCCLS EP5-A guidelines and are presented in the following table:

<table>
<thead>
<tr>
<th>Control</th>
<th>Mean (pg/mL)</th>
<th>Within Run SD</th>
<th>Within Run % CV</th>
<th>Between Run SD</th>
<th>Between Run % CV</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDTA Plasma 1</td>
<td>40.8</td>
<td>1.24</td>
<td>3.1</td>
<td>1.82</td>
<td>4.5</td>
<td>5.4</td>
</tr>
<tr>
<td>EDTA Plasma 2</td>
<td>1343.6</td>
<td>12.89</td>
<td>1.0</td>
<td>89.05</td>
<td>6.6</td>
<td>6.7</td>
</tr>
<tr>
<td>Control Level 1</td>
<td>24.5</td>
<td>0.65</td>
<td>2.7</td>
<td>1.29</td>
<td>5.3</td>
<td>5.9</td>
</tr>
<tr>
<td>Control Level 2</td>
<td>77.2</td>
<td>1.97</td>
<td>2.6</td>
<td>2.49</td>
<td>3.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Control Level 3</td>
<td>3966.2</td>
<td>45.04</td>
<td>1.1</td>
<td>70.90</td>
<td>1.8</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Interfering Substances

Hemoglobin (up to 500 mg/dL), triglycerides (triolein up to 3000 mg/dL), bilirubin (conjugated up to 20 mg/dL), fibrinogen (up to 800 mg/dL) or human serum albumin (up to 1500 mg/dL) added to plasma specimens containing BNP did not interfere with the recovery of BNP.

Analytical Specificity

Pharmaceuticals

The following drugs were evaluated for potential cross-reactivity and interference in the Alere Triage® BNP test. All drugs were tested at concentrations representing the blood concentrations that would result from a maximal therapeutic dose and at least twice the maximal therapeutic dose. None of the drugs interfered with the recovery of BNP. Additionally, these drugs did not produce a significant response when tested in a specimen not containing BNP. There was no significant interference with the BNP measurement, nor was there any assay cross-reactivity.

<table>
<thead>
<tr>
<th>Acetaminophen</th>
<th>Cocaine</th>
<th>Nitrofurantoin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>Diclofenac</td>
<td>Nystatin</td>
</tr>
<tr>
<td>Ambroxol</td>
<td>Digoxin</td>
<td>Oxytetracycline</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Dopamine</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>Erythromycin</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Furosemide</td>
<td>Quinidine</td>
</tr>
<tr>
<td>Atenol</td>
<td>Heparin</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Ibuprofen</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Captopril</td>
<td>Methyldopa</td>
<td>Verapamil</td>
</tr>
<tr>
<td>Cinnarazine</td>
<td>Nifedipine</td>
<td></td>
</tr>
</tbody>
</table>

Nesiritide is a synthetic form of BNP; BNP measurements should not be performed during Nesiritide Infusion.
Proteins and Peptides
The following proteins and peptides were evaluated for potential cross-reactivity and interference in the Alere Triage® BNP test at the concentrations indicated below. There was no significant interference with the BNP measurement, nor was there any significant assay cross-reactivity.

Reactivity with Related Proteins and Peptides

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration of Substance</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenomedullin</td>
<td>1000 pg/mL</td>
<td>101.4%</td>
</tr>
<tr>
<td>α Atrial Natriuretic polypeptide 1-28</td>
<td>1000 pg/mL</td>
<td>99.2%</td>
</tr>
<tr>
<td>Angiotensin I</td>
<td>600 pg/mL</td>
<td>97.9%</td>
</tr>
<tr>
<td>Angiotensin II</td>
<td>600 pg/mL</td>
<td>96.5%</td>
</tr>
<tr>
<td>Angiotensin III</td>
<td>1000 pg/mL</td>
<td>95.1%</td>
</tr>
<tr>
<td>Arg Vasopressin</td>
<td>1000 pg/mL</td>
<td>95.7%</td>
</tr>
<tr>
<td>C type Natriuretic Peptide 53</td>
<td>1000 pg/mL</td>
<td>96.8%</td>
</tr>
<tr>
<td>Endothelin I</td>
<td>20 pg/mL</td>
<td>99.2%</td>
</tr>
<tr>
<td>Prepro ANF 104-123</td>
<td>1000 pg/mL</td>
<td>96.7%</td>
</tr>
<tr>
<td>Prepro ANF 26-55</td>
<td>1000 pg/mL</td>
<td>94.2%</td>
</tr>
<tr>
<td>Prepro ANF 56-92</td>
<td>1000 pg/mL</td>
<td>95.6%</td>
</tr>
<tr>
<td>Prepro BNP 1-21</td>
<td>1000 pg/mL</td>
<td>98.5%</td>
</tr>
<tr>
<td>Prepro BNP 22-46</td>
<td>1000 pg/mL</td>
<td>97.7%</td>
</tr>
<tr>
<td>Renin</td>
<td>50 ng/mL</td>
<td>95.8%</td>
</tr>
<tr>
<td>Urodilatin 95-126</td>
<td>1000 pg/mL</td>
<td>91.6%</td>
</tr>
</tbody>
</table>

Analytical Sensitivity
The lowest detectable level of BNP distinguishable from zero (Alere Triage® BNP Calibrator S0) with 95% confidence is 1 pg/mL. This value is determined by processing a complete six point calibration curve, controls, and 10 replicates of the zero calibrator in multiple assays. The analytical sensitivity value is calculated from the curve at the point that is two standard deviations from the mean zero calibrator signal.

Data from Clinical Studies
Individuals Without CHF
The circulating BNP concentration was determined from 1286 individuals without CHF (676 women and 610 men). This population included individuals with hypertension, diabetes, renal insufficiency, and chronic obstructive pulmonary disease. There are no statistically significant changes in BNP concentration associated with hypertension, diabetes, renal insufficiency, and chronic obstructive pulmonary disease. The descriptive statistics for BNP concentrations in individuals without CHF are shown in the table below. The values are representative of the values obtained from clinical studies. The decision threshold was determined by the 95% confidence limit of BNP concentration in the non-CHF population age 55 and older. The most appropriate decision threshold apparent from these distributions is 100 pg/mL. This value translates into a general specificity of the test of 98%, i.e. less than 2% expected false positives in individuals without CHF. Each laboratory should establish a reference range that represents the patient population that is to be evaluated.

Descriptive Statistics – BNP Concentration (pg/mL) Non-CHF Population

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Age &lt; 45</th>
<th>Age 45-54</th>
<th>Age 55-64</th>
<th>Age 65-74</th>
<th>Age 75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>12.3</td>
<td>7.7</td>
<td>11.1</td>
<td>17.9</td>
<td>19.8</td>
<td>53.9</td>
</tr>
<tr>
<td>95th Percentile</td>
<td>73.5</td>
<td>39.6</td>
<td>64.5</td>
<td>76.1</td>
<td>84.7</td>
<td>179.4</td>
</tr>
<tr>
<td>Percent &lt; 100 pg/mL</td>
<td>98.0%</td>
<td>99.5%</td>
<td>99.2%</td>
<td>97.4%</td>
<td>96.9%</td>
<td>84.2%</td>
</tr>
<tr>
<td>Minimum</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>252.0</td>
<td>251.3</td>
<td>252.0</td>
<td>207.7</td>
<td>197.9</td>
<td>218.5</td>
</tr>
<tr>
<td>N</td>
<td>1286</td>
<td>423</td>
<td>385</td>
<td>229</td>
<td>192</td>
<td>57</td>
</tr>
</tbody>
</table>

Males

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Age &lt; 45</th>
<th>Age 45-54</th>
<th>Age 55-64</th>
<th>Age 65-74</th>
<th>Age 75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>7.1</td>
<td>5.0</td>
<td>7.2</td>
<td>9.0</td>
<td>15.7</td>
<td>39.0</td>
</tr>
<tr>
<td>95th Percentile</td>
<td>56.9</td>
<td>23.8</td>
<td>39.0</td>
<td>72.4</td>
<td>62.7</td>
<td>77.9</td>
</tr>
<tr>
<td>Percent &lt; 100 pg/mL</td>
<td>98.9%</td>
<td>98.9%</td>
<td>99.5%</td>
<td>98.3%</td>
<td>98.9%</td>
<td>95.8%</td>
</tr>
<tr>
<td>Minimum</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>252.0</td>
<td>251.3</td>
<td>252.0</td>
<td>207.7</td>
<td>127.3</td>
<td>218.5</td>
</tr>
<tr>
<td>N</td>
<td>610</td>
<td>183</td>
<td>196</td>
<td>118</td>
<td>89</td>
<td>24</td>
</tr>
</tbody>
</table>

Females

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Age &lt; 45</th>
<th>Age 45-54</th>
<th>Age 55-64</th>
<th>Age 65-74</th>
<th>Age 75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>18.5</td>
<td>11.6</td>
<td>17.7</td>
<td>28.2</td>
<td>27.6</td>
<td>67.1</td>
</tr>
<tr>
<td>95th Percentile</td>
<td>84.2</td>
<td>47.4</td>
<td>71.7</td>
<td>80.5</td>
<td>95.4</td>
<td>179.5</td>
</tr>
<tr>
<td>Percent &lt; 100 pg/mL</td>
<td>97.2%</td>
<td>100.0%</td>
<td>98.9%</td>
<td>96.4%</td>
<td>95.1%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Minimum</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>197.9</td>
<td>92.6</td>
<td>142.8</td>
<td>143.2</td>
<td>197.9</td>
<td>194.1</td>
</tr>
<tr>
<td>N</td>
<td>676</td>
<td>240</td>
<td>189</td>
<td>111</td>
<td>103</td>
<td>33</td>
</tr>
</tbody>
</table>
Individuals with CHF

Blood samples were obtained from 804 patients diagnosed with CHF (246 women and 558 men). The descriptive statistics for BNP concentrations in patients with CHF are presented in the table below. These values are representative of the values obtained from clinical studies. Each laboratory should establish a reference range that represents the patient population that is to be evaluated. In addition, laboratories should be aware of their respective institutions' current practice for the evaluation of patients with CHF.

CHF Population – All

<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (ng/mL)</td>
<td>359.5</td>
<td>95.4</td>
<td>221.5</td>
<td>459.1</td>
</tr>
<tr>
<td>5th Percentile (ng/mL)</td>
<td>22.3</td>
<td>14.8</td>
<td>9.9</td>
<td>37.6</td>
</tr>
<tr>
<td>Percent &gt; 100 pg/mL</td>
<td>80.6%</td>
<td>48.3%</td>
<td>76.6%</td>
<td>86.0%</td>
</tr>
<tr>
<td>Minimum (ng/mL)</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Maximum (ng/mL)</td>
<td>&gt;5000</td>
<td>904.6</td>
<td>4435.8</td>
<td>&gt;5000</td>
</tr>
<tr>
<td>N</td>
<td>804</td>
<td>118</td>
<td>197</td>
<td>300</td>
</tr>
</tbody>
</table>

CHF Population – Males

<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (ng/mL)</td>
<td>317.8</td>
<td>87.8</td>
<td>232.6</td>
<td>458.9</td>
</tr>
<tr>
<td>5th Percentile (ng/mL)</td>
<td>21.9</td>
<td>16.8</td>
<td>10.7</td>
<td>25.0</td>
</tr>
<tr>
<td>Percent &gt; 100 pg/mL</td>
<td>78.9%</td>
<td>46.5%</td>
<td>78.8%</td>
<td>85.2%</td>
</tr>
<tr>
<td>Minimum (ng/mL)</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Maximum (ng/mL)</td>
<td>&gt;5000</td>
<td>904.6</td>
<td>2710.6</td>
<td>&gt;5000</td>
</tr>
<tr>
<td>N</td>
<td>558</td>
<td>101</td>
<td>146</td>
<td>203</td>
</tr>
</tbody>
</table>

CHF Population – Females

<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (ng/mL)</td>
<td>499.7</td>
<td>114.7</td>
<td>191.2</td>
<td>469.2</td>
</tr>
<tr>
<td>5th Percentile (ng/mL)</td>
<td>30.7</td>
<td>6.8</td>
<td>9.7</td>
<td>45.6</td>
</tr>
<tr>
<td>Percent &gt; 100 pg/mL</td>
<td>84.6%</td>
<td>58.8%</td>
<td>70.6%</td>
<td>87.6%</td>
</tr>
<tr>
<td>Minimum (ng/mL)</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>11.7</td>
</tr>
<tr>
<td>Maximum (ng/mL)</td>
<td>&gt;5000</td>
<td>519.6</td>
<td>4435.8</td>
<td>4582.0</td>
</tr>
<tr>
<td>N</td>
<td>246</td>
<td>17</td>
<td>51</td>
<td>97</td>
</tr>
</tbody>
</table>

*2 CHF with unknown NYHA Functional Class (male)

The New York Heart Association (NYHA) developed a four-stage functional classification system for CHF that is based on a subjective interpretation of the severity of a patient’s clinical signs and symptoms. Class I patients have no limitations of physical activity and have no symptoms with ordinary physical activity. Class II patients have a slight limitation of physical activity and have symptoms with ordinary physical activity. Class III patients have a marked limitation of physical activity and have symptoms with less than ordinary physical activity, but not at rest. Class IV patients are unable to perform any physical activity without discomfort. Reports in the scientific literature have indicated that there is a relationship between BNP and the severity of CHF. An analysis of NYHA classification and BNP concentrations from the clinical study data indicate that there is a relationship between the severity of the clinical signs and symptoms of CHF and BNP concentration. These data are consistent with the previous reports in the literature, and further demonstrate that BNP measurements, along with NYHA classification, can provide additional objective information to the physician about the patient's CHF severity.
Diagnostic Utility

Various studies have demonstrated that circulating BNP concentrations increase with the severity of CHF based on the NYHA classification. BNP concentrations are much lower than ANP concentrations normally, but as the severity of CHF advances according to the NYHA classification, plasma BNP increases progressively more than respective ANP values⁶. Therefore, BNP is a more useful marker than ANP to distinguish between normal subjects and patients in the earlier stages of CHF. BNP is more sensitive and specific than ANP for detecting decreases in LVEF⁷,¹⁶. Additionally, there is a positive correlation between blood BNP concentrations and left ventricular end diastolic pressure and inverse correlation to left ventricular function following acute myocardial infarction¹⁶. Blood BNP concentrations represent an independent assessment of ventricular function without the use of other invasive or expensive diagnostic tests¹⁶. There is an association with elevated BNP concentrations and alterations in hemodynamic parameters including raised atrial and pulmonary wedge pressures, reduced ventricular systolic and diastolic function, left ventricular hypertrophy, and myocardial infarction¹⁹. Numerous reports in the scientific literature have described the utility of BNP as a diagnostic marker for CHF and left ventricular dysfunction¹,²,⁷,¹⁶-²³. These observations are supported by an analysis of the clinical study data. The Receiver Operating Characteristic (ROC) Curve of BNP cut-offs versus clinical sensitivity and specificity from the clinical study data is provided below. The area under the curve is 0.955 ± 0.005. The clinical utility of the Alere Triage® BNP test also has been confirmed and described in detail in the scientific literature²⁴,²⁵.

A box and whiskers plot for the clinical study population is provided below, with a horizontal dashed line representing the suggested cutoff of 100 pg/mL.
The clinical sensitivity and specificity of the Alere Triage® BNP Test using a cutoff of 100 pg/mL for various age groups within each gender is described in the table below.

### Males

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sensitivity</th>
<th>95% Confidence Interval</th>
<th>Specificity</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 45</td>
<td>81.6%</td>
<td>70.8-92.5%</td>
<td>98.9%</td>
<td>97.4-100.0%</td>
</tr>
<tr>
<td>Age 45-54</td>
<td>76.0%</td>
<td>67.5-84.6%</td>
<td>99.5%</td>
<td>98.5-100.0%</td>
</tr>
<tr>
<td>Age 55-64</td>
<td>75.6%</td>
<td>68.2-82.9%</td>
<td>98.3%</td>
<td>97.7-98.9%</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>79.3%</td>
<td>72.6-86%</td>
<td>98.9%</td>
<td>98.4-99.4%</td>
</tr>
<tr>
<td>Age 75+</td>
<td>82.4%</td>
<td>76.1-88.7%</td>
<td>95.8%</td>
<td>94.7-96.9%</td>
</tr>
</tbody>
</table>

### Females

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sensitivity</th>
<th>95% Confidence Interval</th>
<th>Specificity</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 45</td>
<td>82.1%</td>
<td>68.0-96.3%</td>
<td>100.0%</td>
<td>100.0-100.0%</td>
</tr>
<tr>
<td>Age 45-54</td>
<td>69.0%</td>
<td>57.1-80.9%</td>
<td>98.9%</td>
<td>97.5-100.0%</td>
</tr>
<tr>
<td>Age 55-64</td>
<td>82.4%</td>
<td>71.9-92.8%</td>
<td>96.4%</td>
<td>95.5-97.4%</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>97.9%</td>
<td>93.7-100.0%</td>
<td>95.0%</td>
<td>93.4-96.7%</td>
</tr>
<tr>
<td>Age 75+</td>
<td>91.9%</td>
<td>85.2-98.7%</td>
<td>75.7%</td>
<td>72.2-79.2%</td>
</tr>
</tbody>
</table>

It has been reported that BNP has excellent utility as an aid in the diagnosis of patients with CHF and preserved systolic function (CHF–PSF), generally referred to as diastolic dysfunction 19,26-28. The diagnostic utility of BNP in CHF–PSF patients was determined from the clinical study data by determining the area under the ROC curve for individuals without CHF versus 155 individuals with CHF that had ejection fractions ≥50%. The area under the curve is 0.934 ± 0.012, which indicates that the test is effective as an aid in the diagnosis of CHF in patients with preserved systolic function.

An age-matched analysis of the clinical data was performed with the following common age distribution in the groups of individuals with and without CHF: individuals less than 35 years old comprise 3% of the total number of observations, individuals age 35–44 comprise 6% of the total, individuals age 45–54 comprise 11% of the total, individuals 55–64 years old comprise 22% of the total, individuals 65–74 years old comprise 26% of the total, and individuals 75 years and older comprise 32% of the total. This age distribution reflects the prevalence of CHF within the age groups and genders, according to data published by the American Heart Association in the 2000 Heart and Stroke Statistical Update, and also reflects the age structure of the United States population, according to data published by the National Center for Health Statistics in Health, United States, 2000. The resulting area under the ROC curve is 0.930 with a 95% confidence interval of 0.902–0.958.

### Prognostic Utility in Patients with Acute Coronary Syndromes

BNP concentrations measured in patients with acute coronary syndromes (ACS) or cardiovascular disease provide prognostic information about the patient's risk for death and the development of CHF 19,29-33. Statistically significant increases in death, future myocardial infarction, and CHF have been associated with higher BNP concentrations measured within the first 72 hours after the onset of ACS symptoms. In a recent clinical study, BNP concentrations were evaluated in an observational, retrospective manner in patients with ACS (consisting of unstable angina, myocardial infarction with ST-segment elevation, or myocardial infarction without ST-segment elevation). BNP measurements were performed on specimens obtained within 72 hours after the onset of ischemic discomfort from a population of 2525 high-risk ACS patients that met standard diagnostic criteria for ACS. Patients whose BNP concentration was at least 80 pg/mL had higher rates of death, myocardial infarction, and CHF both at 30 days and at 10 months after presentation than patients whose BNP concentration was below 80 pg/mL 41. In this population of patients with ACS, BNP measurements within the first 72 hours after the onset of symptoms provide useful predictive information to aid in the risk stratification of patients with ACS.

### Prognostic Utility in Patients with Heart Failure

BNP concentrations measured at admission and/or discharge in patients with heart failure provide prognostic information about the patient's risk for death or rehospitalization. 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, and that admitted heart failure patients whose BNP values did not decrease over the course of their treatment are at a particularly high risk of death or a cardiovascular event 40,41. The authors also found that higher BNP concentrations in asymptomatic patients were prognostic for future death or cardiovascular events. Vrtovec et al and Harrison et al studied heart failure patients at the time of presentation and found that patients with higher BNP concentrations (> 1,000 pg/mL and > 480 pg/mL, respectively) had a significantly higher risk of all-cause, cardiac, and pump-failure death and cardiac-related readmissions 42-44. Cheng et al and Bettencourt et al studied admitted heart failure patients receiving treatment and found that patients who did not experience death or readmission within 30 days or 6 months exhibited a decrease in BNP concentrations from admission to discharge, while patients whose BNP concentration did not decrease from admission to discharge were at significantly higher risk for adverse events 45,46. Logeart et al found that admitted heart failure patients with pre-discharge BNP concentrations of 350-700 pg/mL had a hazard ratio of 5.1 for death or readmission for heart failure within 6 months and patients with a pre-discharge BNP concentration greater than 700 pg/mL had a hazard ratio of 15.2 for the same endpoint compared to patients with a pre-discharge BNP concentration less than 350 pg/mL 47. Taken together, these studies indicate that higher BNP concentrations or the lack of a decrease in the BNP concentration from hospital admission to discharge indicate an increased risk of hospitalization or death in patients with heart failure.
Intended Use
The Alere Triage® BNP QC Controls are intended for monitoring the performance of the Alere Triage® BNP test using the Beckman Coulter Access Family of Immunoassay Systems.

Summary and Explanation
Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of the Alere Triage® BNP test. In addition, they are an integral part of good laboratory practices. When performing the Alere Triage® BNP test, include quality control materials to validate the integrity of the assays. The assayed values should fall within the acceptable range if the test system is working properly.

Product Information
Alere Triage® BNP QC Controls
Cat. No. 98201: 2.5 mL/vial, 2 vials each level
• Provided ready to use.
• Mix contents by gently inverting before use. Avoid bubble formation.
• Stable until the expiration date stated on the label when stored at -20 °C or colder in a non-defrosting freezer away from the freezer door.
• Vial is stable at 2-10 °C for 30 days after initial use or when removed from frozen storage.
• Signs of possible deterioration are control values out of range.
• Refer to the QC value card for mean values and standard deviations (SD).

QC 1, QC 2, QC 3: Recombinant human BNP complex at levels of approximately 80, 400, and 2200 pg/mL (ng/L), respectively, in buffered BSA matrix with surfactant, < 0.1% sodium azide, and 0.1% ProClin® 300.

QCC Value Card: 1

Warnings and Precautions
• For In Vitro Diagnostic Use.
• Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local, state and federal regulations and guidelines.
• Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.

GHS Hazard Classification

H317 May cause an allergic skin reaction.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray
P272 Contaminated work clothing should not be allowed out of the workplace
P280 Wear protective gloves/protective clothing/eye protection/face protection
P302+P352 IF ON SKIN: Wash with plenty of soap and water
P321 Specific treatment (see First aid measures on this label)
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P362+P364 Take off contaminated clothing and wash it before reuse
P501 Dispose of contents/container to [X]

European Hazard Classification

Xi;R43 R43 May cause sensitization by skin contact.
S28 After contact with skin, wash immediately with plenty of soap and water.
S37 Wear suitable gloves.

• The Safety Data Sheet (SDS) is available upon request.
Procedure
Determine the concentration of BNP in the Alere Triage® BNP test QC Controls using the Beckman Coulter Access Family of Immunoassay Systems in the same manner as a patient sample. Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Refer to the appropriate system manuals and/or Help system for information on quality control theory, configuring controls, quality control sample test request entry, and reviewing quality control data.

Limitations of the Procedure
If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

Expected Values
For the value assignment of the Alere Triage® BNP QC Controls, a number of samples, representative of the entire lot, are selected and assayed to provide a reliable estimate of the mean value. The mean values and standard deviations are listed on the QC value card. Variations, such as in technique, equipment, or reagents may result in values different from those listed. Therefore, each laboratory should establish its own mean values and standard deviations (SD).
Intended Use
The Alere Triage® BNP Calibrators are intended to calibrate the Alere Triage® BNP test for the quantitative determination of BNP levels in human EDTA plasma using the Beckman Coulter Access Family of Immunoassay Systems.

Summary and Explanation
Quantitative assay calibration is the process by which samples with known analyte concentrations (i.e., assay calibrators) are tested like patient samples to measure the response. The mathematical relationship between the measured responses and the known analyte concentrations establishes the calibration curve. This mathematical relationship, or calibration curve, is used to convert RLU (Relative Light Unit) measurements of patient samples to specific quantitative analyte concentrations.

Traceability
The measurand (analyte) in the Alere Triage® BNP Calibrators is traceable to the manufacturer’s working calibrators. Traceability process is based on prEN ISO 17511. The assigned values were established using representative samples from this lot of calibrator and are specific to the assay methodologies of the Alere Triage® BNP test reagents. Values assigned by other methodologies may be different. Such differences, if present, may be caused by inter-method bias.

Product Information
Alere Triage® BNP Calibrators
Cat. No. 98202: S0–S5, 1.5 mL/vial
- Provided ready to use.
- Stable until the expiration date stated on the label when stored at -20 °C or colder in a non-defrosting freezer away from the freezer door.
- Vial is stable at 2-10 °C for 30 days after initial use or when removed from frozen storage.
- Signs of possible deterioration are control values out of range.

<table>
<thead>
<tr>
<th>S0:</th>
<th>Buffered bovine serum albumin (BSA) matrix with surfactant, &lt; 0.1% sodium azide, and 0.1% ProClin® 300.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1, S2, S3, S4, S5:</td>
<td>Recombinant human BNP complex at levels of approximately 25, 100, 500, 2500 and 5000 pg/mL in buffered BSA matrix with surfactant, &lt; 0.1% sodium azide, and 0.1% ProClin 300.</td>
</tr>
<tr>
<td>Calibration Card:</td>
<td>1</td>
</tr>
</tbody>
</table>

Warnings and Precautions
- For In Vitro Diagnostic Use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local, state and federal regulations and guidelines.
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.

GHS Hazard Classification

**GXM/MXLH PMP WARNING**

- **H317** May cause an allergic skin reaction.
- **P261** Avoid breathing dust/fume/gas/mist/vapors/spray
- **P272** Contaminated work clothing should not be allowed out of the workplace
- **P280** Wear protective gloves/protective clothing/eye protection/face protection
- **P302+P352** IF ON SKIN: Wash with plenty of soap and water
- **P321** Specific treatment (see First aid measures on this label)
- **P333+P313** If skin irritation or rash occurs: Get medical advice/attention.
- **P362+P364** Take off contaminated clothing and wash it before reuse
- **P501** Dispose of contents/container to [X]

European Hazard Classification

**GXM/MXLH PMP** **WARNING**

- **Xi;R43** May cause sensitization by skin contact.
- **R43** May cause sensitization by skin contact.
- **S28** After contact with skin, wash immediately with plenty of soap and water.
- **S37** Wear suitable gloves.

- The Safety Data Sheet (SDS) is available upon request.
Procedure
Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Calibration Details
The Alere Triage® BNP Calibrators are provided at 6 levels - zero and approximately 25, 100, 500, 2500 and 5000 pg/mL. Assay calibration data are valid up to 28 days.
Run Calibrators in duplicate.

Limitations of the Procedure
If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.
References


Other Suggested Reading


Glossary of Symbols

- Caution, consult accompanying documents
- Use by
- LOT: Batch code
- REF: Catalog number
- Consult instructions for use
- Manufacturer

- EC: Authorized representative in the European Community
- REP: In Vitro diagnostic medical device
- IVD: Store at 2 - 8°C
- 2°C - 8°C: Store at 2 - 8°C
- 2°C - 10°C: Store at 2 - 10°C
- ≤-20°C: Store at -20°C

- CONT: Contents
- CONTROL: Control
- CONTROL 1: Control 1
- CONTROL 2: Control 2
- CONTROL 3: Control 3
- CONTROL: Control
- CAL: Calibrator
- CAL S0: Calibrator S0
- CAL S1: Calibrator S1
- CAL S2: Calibrator S2
- CAL S3: Calibrator S3
- CAL S4: Calibrator S4
- CAL S5: Calibrator S5

- Ag: Antigen
- BNP: B-Type Natriuretic Peptide (BNP)
- Ab: Antibody
- BNP-AP: Alkaline Phosphatase Conjugate
- REAG: Reagent
- REAG 1a: Reagent 1a
- REAG 1b: Reagent 1b
- REAG 1c: Reagent 1c

- CC: Calibration Card
- QCC: Quality Control Card
- ORIG: Origin
- MOU: mouse
- ORIG HUM: human
- ORIG GOAT: goat
- BUF: Buffer

- Recyclable
- This way up
- Average Mean
- Standard Deviation
- CE Mark
- Antibody BNP

- Biological Risks
- Contains sufficient for < n > tests
### Contact Alere

**Alere™ Product Support**

Contact one of the following Alere™ Product Support Care Centers or your local distributor if you have any questions regarding the use of your Alere™ product. You may also contact us at www.alere.com.

<table>
<thead>
<tr>
<th>Region</th>
<th>Phone</th>
<th>E Mail Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe &amp; Middle East</td>
<td>+ 44.161.483.9032</td>
<td><a href="mailto:EMEproductsupport@alere.com">EMEproductsupport@alere.com</a></td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>+ 61.7.3363.7711</td>
<td><a href="mailto:APproductsupport@alere.com">APproductsupport@alere.com</a></td>
</tr>
<tr>
<td>Africa, Russia, &amp; CIS</td>
<td>+ 972.8.9429.683</td>
<td><a href="mailto:ARClISproductsupport@alere.com">ARClISproductsupport@alere.com</a></td>
</tr>
<tr>
<td>Latin America</td>
<td>+ 57.2.6618797</td>
<td><a href="mailto:LAprouductsupport@alere.com">LAprouductsupport@alere.com</a></td>
</tr>
<tr>
<td>Canada</td>
<td>+ 1.613.271.1144</td>
<td><a href="mailto:CANproductsupport@alere.com">CANproductsupport@alere.com</a></td>
</tr>
<tr>
<td>US</td>
<td>+ 1.877.308.8287</td>
<td><a href="mailto:USproductsupport@alere.com">USproductsupport@alere.com</a></td>
</tr>
</tbody>
</table>

### Alere™ Customer Service

Contact the following Alere™ Service Care Center or your local distributor for order and billing assistance. You may also contact us at www.alere.com.

<table>
<thead>
<tr>
<th>Phone</th>
<th>E Mail Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 1.877.441.7440</td>
<td><a href="mailto:clientservices@alere.com">clientservices@alere.com</a></td>
</tr>
</tbody>
</table>
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Revision changes:
- Performed formatting changes throughout document.
- Removed all patent numbers
- Update Copyright year throughout document.