

**Employee Health Alere Triage**

 **Clinic BNP**

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Intended Use

The Quidel Triage BNP Test is a rapid, point of care fluorescence immunoassay to be used with the Quidel Triage Meters for the quantitative measurement of B-type natriuretic peptide (BNP) in EDTA anticoagulated whole blood or plasma specimens. The test is intended to be used as an aid in the diagnosis and assessment of severity of congestive heart failure (also referred to as heart failure). The test also is used for the risk stratification of patients with acute coronary syndromes and for the risk stratification of patients with heart failure.

Summary and Explanation of the Test

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 single use Fluorescence immunoassay device designed to determine the concentration of BNP in EDTA anticoagulated whole blood or plasma specimens.

The test procedure involves the addition of several drops of an EDTA anticoagulated whole blood or plasma specimen to the sample port on the Test Device. After addition of the specimen, the whole blood cells are separated from the plasma using a filter contained in the Test Device. The specimen reacts with fluorescent antibody conjugates and flows through the Test Device by capillary action. Complexes of each fluorescent antibody conjugate are captured on discrete zones specific to the analyte.

The Test Device is inserted into the Quidel Triage Meter (hereafter referred to as Meter). The Meter is programmed to perform the BNP analysis after the specimen has reacted with the reagents within the Test Device. The concentration of BNP in the specimen is directly proportional to the fluorescence detected. The results are displayed on the Meter screen in approximately 15 minutes from the addition of specimen. The analysis is based on the amount of fluorescence the Meter detects within a measurement zone on the Test Device. A greater amount of fluorescence detected by the Meter indicates a higher BNP concentration in the specimen. All results are stored in the Meter memory to display or print when needed. If connected, the Meter can transmit results to the lab or hospital information system.

REAGENTS AND MATERIALS PROVIDED

The Quidel Triage BNP Test contains all reagents necessary for the quantification of BNP in EDTA anticoagulated whole blood or plasma specimens.

The Test Device contains:

* Murine monoclonal antibodies and polyclonal antibodies against BNP.
* Fluorescent dye.
* Stabilizers.

Kit contains:

* 25 Test Devices 25 Transfer Pipettes
* 1 Reagent CODE CHIP Module
* 1 Printer
* Paper Roll

MATERIALS REQUIRED BUT NOT PROVIDED

* Quidel Triage MeterPro Cat. # 55070 or 55071
* Triage MeterPlus Cat. # 55040 or 55041
* Quidel Triage BNP Control 1 Cat. # 98013XR
* Quidel Triage BNP Control 2 Cat. # 98014XR

OR

* Quidel Triage Total 5 Control 1 Cat. # 88753
* Quidel Triage Total 5 Control 2 Cat. # 88754

Warnings and Precautions

* For In Vitro Diagnostic Use.
* For use by healthcare professionals.
* Do not use the kit beyond the expiration date printed on the outside of the box.
* Carefully follow the instructions and procedures described in this insert and the quick reference instruction.
* Optimal results will be achieved by performing testing at temperatures between 20°C to 24°C (68°F to 75°F).
* If results from multiple specimens from the same patient will be compared, it is recommended to maintain a consistent sample type (whole blood or plasma)
* Sample dilution is not recommended.
* The use of non-Quidel Controls and Calibration Verification materials is not recommended.
* Keep the Test Device in the sealed pouch until ready for immediate use. Discard after single use
* The transfer pipette should be used for one patient specimen only. Discard after single use.
* Patient specimens, used Test Devices and used transfer pipettes may be potentially infectious. Proper handling and disposal methods should be established by the laboratory in accordance with local, state and federal regulations.
* The Quidel 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 result.
* 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.

**Storage and Handling Requirements**

* Store the Test Devices in a refrigerator at 2°-8° C (35°-46°F).
* Once removed from refrigeration, the pouched test device is stable for up to 14 days at room temperature, but not beyond the expiration date printed on the pouch. With a soft felt tip marker, gently write the date and time of removal from the refrigerator on the pouch and cross out the manufacturer expiration date printed on the pouch. Care must be taken to document the time the product is at room temperature. Once equilibrated to room temperature, do not return the test device to refrigeration.
* Before using refrigerated Test Devices, allow individual foil pouches to reach operating temperature (20°-24° C or 68°-46°F). This will take a minimum of 15 minutes. If a kit containing Multiple Test Devices is removed from refrigeration, allow the kit to reach room temperature before use. This will take a minimum of 60 minutes.
* Do not remove the Test Device from the pouch until prepared for immediate use.

**Specimen Collection and Preparation**

A venous whole blood or plasma specimen using EDTA as the anticoagulant is required for testing with this product. Other blood specimen types have not been evaluated. Use of plastic blood draw tubes containing K2 EDTA as an anticoagulant for sample collection permits an accurate measurement of plasma BNP concentrations (Davidson et al. Cirulation 91: 1276, 1995)

For sample collection, follow the sample tube manufacturer’s recommended procedure.

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.

If testing cannot be completed within 24 hours, the plasma should be separated and stored at -20°C until it can be tested. No more than a single freeze/thaw cycle is recommended.

Avoid using severely hemolyzed specimens, whenever possible. If a specimen appears to be severely hemolyzed, another specimen should be obtained and tested.

**Test Procedure**

**Lot Calibration Using the Reagent CODE CHIP™Module**

When a new lot of a Test Devices is opened, the calibration and expiration data for that lot of Test Devices must be transferred to the Meter before patient testing. Use the Reagent CODE CHIP™ module supplied with the new lot of Test Devices to transfer the data to the Meter.

**Perform one time for each new lot of Test Devices**

1. From the main screen, select the **Install New Code Chip.** Press **Enter.**
2. Place the Reagent CODE CHIP™ module into the lower left front corner of the Meter and follow the prompts on the screen.
3. Remove the Reagent CODE CHIP™ module from the Meter when data transfer is complete.
4. Place the Reagent CODE CHIP™ module back into its original container for storage.

**Testing Patient Specimens**

**Procedural Notes**

* For each day of patient testing, perform QC Device testing. Refer to the Quality Control Considerations, section.
* Frozen plasma and refrigerated whole blood or plasma specimens must be allowed to reach room temperature and e mixed thoroughly before testing.
* Mix whole blood specimens by gently inverting the tube several times.
* Mix plasma specimens by vortexing or inverting the tube several times.

**Step 1- Add Patient Specimen**

1. Open the pouch and label the Test device with the patient identification number.

***NOTE: Do not use fluorescent or brightly colored ink, or write outside of the blank area as this may interfere with the test.***

1. Place the Test Device on a level, horizontal surface.
2. Using the transfer pipette, squeeze the larger (top) bulb completely and insert the tip into the specimen.
3. Release the bulb slowly. The transfer pipette barrel should fill completely with some fluid flowing in the smaller (lower) bulb.

***NOTE: Ensure that the pipette is not under filled or over filed. An under filled pipette is one where the barrel is not filled completely with specimen and there is no specimen in the lower bulb. An over filled pipette is one where there is some specimen in the top bulb. Ideally the lower bulb should contain a small amount of specimen (less than one quarter the volume of the lower bulb).***

1. Place the tip of the transfer pipette into the sample port of the Test Device and squeeze the larger bulb completely. The entire volume of fluid in the transfer pipette barrel must flow into the sample port. The specimen in the smaller (lower) bulb should not be expelled.

***Note: Too much specimen has been added to the device if the specimen has migrated outside of the sample port and on to the label.***

1. Remove the transfer pipette tip from the sample port and then release the larger (top) bulb.
2. Discard the transfer pipette
3. Allow the specimen to absorb completely before moving the Test Device. At a minimum the sample should be below the sample port opening to be considered fully absorbed.

**STEP 2- Run Test**

1. From the main screen, select **Run Test** and press **Enter.**
2. Select **Patient Sample** and press **Enter.**
3. Enter the patient identification number and press Enter.
4. Confirm that the number was entered correctly by selecting **Confirm Patient ID** and pressing Enter. If the number was not entered correctly, select **Correct Patient ID**, press **Enter** and repeat the previous step.
5. Holding the Test Device by the edges, insert the Test Device into the Meter and press **Enter**. The result will be displayed when the analysis is complete.

***NOTE: The Test Device must be inserted into the Meter within 30 minutes from the time the patient specimen was added. A delay longer than 30 minutes may cause the results to be invalid and blocked out on the printout.***

**Step 3- Read the Results**

1. Results may be printed by pressing the **Print** button.
2. Discard the Test Device after release from the Meter.
3. A blocked out result indicates the result was invalid and the test should be repeated.

**Results**

The Meter measures the target analyte automatically. The result is displayed on the screen. The operator has the option to print the results. A number in pg/mL represents the amount of the BNP present in the sample.

For additional information, refer to the Alere Triage® Meter User Manual.

The BNP range reported by the test system is 5 pg/mL to 5000 pg/mL.

**Standardization:**

The Alere Triage® BNP Test has been standardized using a purified protein preparation of BNP based on the mass (concentration) of the analyte present in EDTA anticoagulated plasma.

**Quality Control Considerations:**

Every Alere Triage® BNP Test is a quantitative test that includes two internal control materials of different concentrations that are run automatically with every patient specimen, external liquid control solution, or proficiency testing sample. If the automatic check of these built-in controls shows that the control value results are within the limits set during manufacturing, the Meter will report a result for the specimen being tested. If the automatic check of these built-in controls shows that the control value results are not within the limits set during manufacturing, a test result will not be reported. Instead, the Meter will display a warning or error message that is described in the Alere Triage® Meter User Manual.

Good Laboratory Practice suggests that external controls should be tested with each new lot or shipment of test materials, or every 30 days, as otherwise required by your laboratory’s standard quality control procedures. Controls should be tested in the same manner as if testing patient specimens. When running patient specimens or external controls, if an analyte fails for any reason (built in control failure or an external control out of range) no patient results will be reported. Users should follow government guidelines (for example, federal, state or local) and/or accreditation requirements for quality control.

**Performing Alere Triage® System Quality Control- QC Device**

Use the QC Device to ensure proper function of the Meter. Perform QC Device testing for the following conditions:

* Upon initial setup of the Meter
* Each day of patient testing.
* When the Meter has been transported or moved
* Whenever there is uncertainty about the performance of the Meter.
* Whenever required by your laboratory’s quality control requirements.

Do not discard the Alere Triage® QC Device and associated CODE CHIP™ module. Store them in the QC Device box.

Refer to the Alere Triage® User Manual for complete instructions on use of the QC Device.

1. The first time a new QC Device is run in the Meter, install the QC Device CODE CHIP™ module. The QC Device CODE CHIP™ module data is stored in the Meter memory. The QC Device CODE CHIP™ module does not need to be reinstalled after the first time.
	1. From the main screen, select **Install New Code Chip** and press **Enter.**
	2. Place the QC Device CODE CHIP™ module in the lower left front corner of the meter. Follow the prompts on the screen.
	3. Remove the QC Device CODE CHIP™ module from the Meter when data transfer is complete.
	4. Place the QC Device CODE CHIP™ module back into the QC Device Box for storage.
2. From the main screen, select **Run Test** and press **Enter**.
3. If User Id is enabled enter your User ID number and press **Enter**.
4. Select **QC Device** and press **Enter**.
5. Insert QC Device into the Meter and press **Enter**.
6. A Pass or Fail result will be displayed/printed when complete. Each parameter should pass before patient testing is performed.
7. Remove the QC Device from the Meter and place in the QC Device Box. **DO NOT DISCARD THE QC DEVICE.**

*NOTE: If the QC Device or external controls do not perform as expected, review the above instructions to see if the test was performed correctly, repeat the test or contact Alere or your local Alere representative(refer to Contact Alere section). Refer to the Alere Triage® Meter User Manual for a complete description of the quality control system.*

**CLIA Considerations**

The Alere Triage® BNP Test is a CLIA-waived test system for whole blood only. Each laboratory or testing site using the Alere Triage® BNP Test must have a CLIA Certificate of Waiver before starting testing. To obtain a Certificate of Waiver, call your state department of health or contact Alere for an application (form CMS-116). Alere San Diego, Inc., can provide a phone number of your state department of health and assist you in filling out the application. The Alere Triage® BNP Test is a waived test so long as it is used according to the instructions set in the Package Insert. Any modification by the laboratory to the test system or the test system instructions will result in this test no longer meeting the requirements for waived categorization. A modified tests is considered to be high complexity and is subject to all applicable CLIA requirements.

**Results of Untrained User Study:**

An “untrained user” study was conducted in which participants were given only the test instructions and asked to perform testing of three (3) prepared samples at three different BNP levels (low, medium, and high) in random order. The participants were not given any training on the use of the test. A total of 65 participants were enrolled from 3 sites, representing a diverse demographic (educational, age, gender) population.

The table below presents the summary of the performance by the untrained users



A physician office laboratory (POL) study was conducted at four physician offices using 60 EDTA-anticoagulated whole blood samples from apparently healthy volunteers. Each sample was tested by two physician office employees and by a trained laboratory professional. Results from the POL employees were compared to the trained laboratory professional’s results using a Deming regression. The results of the regression analysis were the following: slope=1.01 with 95% Confidence Interval: 0.97 to 1.04; intercept=0.4 with 95% Confidence Interval: -0.4 to 1.1. The average coefficient of variation for the two measurements on each sample by the POL employees for the BNP range of 5 pg/mL to 78 pg/mL was 13.5%.

**Limitations of the Procedure:**

* Test results should be evaluated in the context of all clinical and laboratory data available. In those instances where test results do not agree with the clinical evaluation, additional tests should be performed accordingly.
* Severely hemolyzed specimens should be avoided. When a sample appears to be severely hemolyzed, another specimen should be obtained and tested.
* This test has been evaluated with venous whole blood and plasma using EDTA as the anticoagulant. Other specimen types, draw methods, and anticoagulants have not been evaluated. Use Standard venipuncture techniques. Follow the sample collection recommendations of the sample tube manufacturer.
* There is the possibility that factors such as technical or procedural errors, as well as interfering or cross-reacting substances in patient specimens, may impact the test and cause erroneous results.
* These assays are fluorescence immunoassays and may be affected by environmental conditions. Therefore, it is important for each laboratory to establish its own reference range based on the laboratory conditions and procedures.

Expected Values:

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 of an acute coronary syndrome are associated within 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.

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

**Performance Characteristics:**

**Linearity**

Plasma specimens anticoagulated with EDTA from four apparently healthy individuals were spiked with purified BNP to final concentrations of 5000 pg/mL. Each spiked plasma specimen was diluted gravimetrically with unspiked plasma to obtain BNP values throughout the range of the Alere Triage® BNP Test. Linear regression analysis of the data indicates that the assay is linear throughout the measurable range of the test. Recovery data representing results from nine measurements are shown below



**Analytical Sensitivity**

The analytical sensitivity or lowest detectable concentration that is distinguishable from zero for the Alere Triage® BNP Test was determined by testing a zero calibrator 20 times each using 3 lots of reagents and 5 Meters on 5 days. The average 95% confidence limit of the analytical sensitivity of the Alere Triage® BNP Test was less than 5 pg/mL.

**Interfering Substances**

Hemoglobin (up to 1,000 mg/dL), lipids (cholesterol up to 1,000 mg/dL and triglycerides up to 1,000 mg/dL) or bilirubin (up to 20 mg/dL) added to plasma specimens containing BNP did not interfere with the recovery of BNP. The hematocrit was varied between 27% and 51% with no significant effect on 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. There was no significant interference with the BNP measurement, nor was there any assay cross-reactivity. 

**Proteins and Peptides**

The following proteins and peptides were evaluated for potential cross-reactivity and interference with 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.





**Precision**

The average within-day and total precision were determined using the ANOVA model by testing control materials that had BNP added at concentrations near the decision points of the assay and throughout the range of the standard curve. The study was conducted over 12 days, testing each control 10 times per day. Each Test Device was read on five Alere Triage® Meters. Of particular note, the use of different Meters does not significantly affect the test precision.

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**Other Suggested Reading**

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