**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

**A. 510(k) Number:**

k072189

**B. Purpose for Submission:**

New device and instrument

**C. Measurand:**

N-terminal pro-brain natriuretic peptide

**D. Type of Test:**

Quantitative

**E. Applicant:**

Mitsubishi Kagaku Iatron Inc.

c/o Polymedco Inc.

**F. Proprietary and Established Names:**

 PATHFAST NTproBNP test

**G. Regulatory Information:**

1. Regulation section:

   21 CFR 862.1117, B-type natriuretic peptide

2. Classification:

   Class II

3. Product code:

   NBC

4. Panel:

   75, Chemistry

## H. Intended Use:

1. Intended use(s):

   See Indications for Use below

2. Indication(s) for use:

   PATHFAST NTproBNP test is an in vitro diagnostic test for the quantitative measurement of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) in heparinized or EDTA whole blood and plasma. Measurements of NT-proBNP are used to assist in the diagnosis and assessment of severity of congestive heart failure (CHF) and risk stratification in patients with acute coronary syndrome (ACS). Measurements of NT-proBNP may also be used to assess increased risk of cardiovascular events and mortality in patients with stable coronary artery disease. PATHFAST NTproBNP is for use in clinical laboratory and point of care settings.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   PATHFAST® Analyzer

## I. Device Description:

The PATHFAST NTproBNP test is supplied as a reagent kit. Each kit contains sufficient materials for 60 determinations. The calibrator materials are included with the reagent kit.

**Contents of the PATHFAST NTproBNP reagent kit:**

| Component | Quantity |
|---|---|
| Reagent Cartridge | 6 cartridges x 10 trays |
| Calibrator 1 | 2 vials of 1.0 ml each |
| Calibrator 2 | 2 vials |
| Calibrator diluent | 2 vials of 1.0 ml each |

The reagent cartridge contains 16 wells. Wells 1, 6, 8, 9, 10, 12, 14, 15, 16 are empty. The other wells are filled with the following reagents:

| Reagent Description | Volume | Cartridge Well |
|---|---|---|
| Alkaline phosphatase (microorganism) conjugated anti NT-proBNP polyclonal antibody (sheep) in MOPS buffer with Micr-O-protect (Roche) as preservative | 50 µl | 2 |
| Washing Buffer: MOPS buffer (pH 7.5) with 0.05% sodium azide as preservative | 400 µl | 3, 4, 5 |
| Magnetic particles coated with anti NT-proBNP polyclonal antibody (sheep) in MOPS buffer | 50 µl | 7 |
| Sample Dilution Buffer: MOPS buffer (pH 7.0) with IgG (sheep), and Micr-O-protect as preservative | 25 µl | 11 |
| Chemiluminescent substrate: CDP-Star (Applied Biosystems) | 100 µl | 13 |

Calibrators
o Calibrator 1: Saline solution with 0.05% sodium azide as preservative
o Calibrator 2: Lyophilized preparation containing NT-proBNP, BSA, and preservative
o Calibrator diluent: Aqueous solution with 0.05% sodium azide.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

   Roche Elecsys proBNP assay

2. Predicate 510(k) number(s):

   k051382

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| Item | Device | Predicate |
| Traceability | To reference standards prepared from pure NT-proBNP (1-76) | To reference standards prepared from pure NT-proBNP (1-76) |
| Result interpretation | <75 years: 125 pg/ml ≥75 years: 450 pg/ml | <75 years: 125 pg/ml ≥75 years: 450 pg/ml |

| Differences | | |
|---|---|---|
| Item | Device | Predicate |
| Interfering substances | No interference observed with bilirubin-conjugated and free (60 mg/dL); hemoglobin (1400 mg/dl); lipemia (3000 FTU); rheumatoid factor (1500 IU/mL); triglyceride (1000 mg/dL) | No interference observed with bilirubin-icterus (35 mg/dL); hemoglobin (1400 mg/dL); rheumatoid factor (1500 IU/mL); triglyceride (4000 mg/dL) |
| Indications for use | PATHFAST NTproBNP test is an in vitro diagnostic test for the quantitative measurement of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) in heparinized or EDTA whole blood and plasma. Measurements of NT-proBNP are used to assist in the diagnosis and assessment of severity of congestive heart failure (CHF) and risk stratification in patients with acute coronary syndrome (ACS). Measurements of NT-proBNP may also be used to assess increased risk of cardiovascular events and mortality in patients with stable coronary artery disease. PATHFAST NTproBNP is for use in clinical laboratory and point of care settings. | Elecsys proBNP is used as an aid in the diagnosis of individuals suspected of having congestive heart failure. The test is further indicated for the risk stratification of patients with acute coronary syndrome or congestive heart failure. The test may also serve as an aid in assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease. |
| Sample type | Whole blood, plasma | Serum, plasma |

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

Clinical and Laboratory Standards Institute (CLSI) Documents EP5-A2, EP6-A, EP9-A2, EP 17-A, C28-A2

Class II Special Controls Guidance Document for B-Type Natriuretic Peptide Premarket Notifications: Final Guidance for Industry and FDA Reviewers (11/30/2000).

**L. Test Principle:**

The PATHFAST NTproBNP procedure is based on CLEIA (Chemi-luminescence Enzyme Immuno-Assay). The PATHFAST instrument utilizes Magtration® technology for Bound/Free (B/F) separation in several reaction steps. In this procedure, alkaline phosphatase labeled anti NT-proBNP polyclonal antibody and anti NT-proBNP polyclonal antibody coated magnetic particles are mixed with sample. NT-proBNP contained in the specimen binds to the anti NT-proBNP antibodies forming an immunocomplex with enzyme labeled antibody and antibody coated magnetic particles. After removing the unbound enzyme labeled antibody, a chemiluminescent substrate is added to the immunocomplex. After a short incubation, the luminescence generated by the enzyme reaction is detected. The intensity of the measured luminescence is in relationship with the NT-proBNP concentration in the specimen which is calculated by means of a standard curve.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

   a. *Precision/Reproducibility:*

   Four plasma samples were assayed in duplicate for 20 days. The within-run and total imprecision were calculated according to CLSI EP5-A2. Three PATHFAST instruments were used and the study was done in-house.

| Sample | | Within-run precision | | Total precision | |
|--------|-------------|-------------|--------|-------------|--------|
| | Mean (pg/mL) | SD (pg/mL) | CV (%) | SD(pg/mL) | CV (%) |
| 1 | 101 | 4.14 | 4.1 | 4.72 | 4.7 |
| 2 | 425 | 13.2 | 3.1 | 14.5 | 3.4 |
| 3 | 2388 | 97.0 | 4.1 | 111 | 4.6 |
| 4 | 12058 | 564 | 4.7 | 648 | 5.4 |

   Intra-assay precision was assessed with whole blood samples at three levels of the test. One sample was in the normal range of the test and two above. The results are summarized in the table below:

| Replicate | Level 1 | Level 2 | Level 3 |
|:---:|:---:|:---:|:---:|
| Mean (pg/ml) | 84.3 | 2320 | 12104 |
| SD | 4.13 | 86.5 | 608 |
| %CV | 4.9 | 3.7 | 5.0 |

**Summary of Point of Care Testing**

Testing with the PATHFAST NTproBNP test was performed in 3 non-laboratory sites. Personnel recruited to perform the testing were physician assistants and medical office personnel. Three types of testing were performed at each site: precision testing at 2 levels of the test; precision testing of whole blood samples; comparison with predicate method. Testing was performed at each site over 5 days. Two operators performed the testing at each site. Four PATHFAST instruments were used. The sponsor's acceptance criterion was day to day and between site precision CV less than 10 %.

|  | Site 1 | Site 2 | Site 3 |
|---|---|---|---|
| Mean | 315 | 299 | 323 |
| SD | 24.7 | 15.1 | 17.3 |
| CV | 7.8% | 5.0% | 5.3% |

|  | Site 1 | Site 2 | Site 3 |
|---|---|---|---|
| Mean | 10073 | 10686 | 11699 |
| SD | 243.8 | 765.4 | 309.8 |
| CV | 2.4% | 7.2% | 2.6% |

Whole blood precision testing was performed on lithium heparin whole blood tested in duplicate. At least 10 samples were tested at each site. Some samples were spiked with control material to obtain elevated samples. Samples tested at Site 1 had NT-proBNP levels ranging from 62 to 346 pg/mL with % CV for the duplicates ranging from 0.4 to 5.6%; samples tested at Site 2 had levels ranging from 45 to 1972 pg/mL with % CV ranging from 0.3 to 5.6%; samples tested at Site 3 had levels ranging from 17.5 to 4777 pg/mL with % CV ranging from 0.0 to 3.9 %. Samples with values near the cutoffs of 125 and 450 pg/mL were included and the % CV ranged from 0.4 to 5.6 %.

b. *Linearity/assay reportable range:*

A sample at the upper limit of the test range was prepared by spiking NT-proBNP free human heparinized plasma with NT-proBNP antigen. The prepared sample was then diluted to nine additional levels with the plasma. Each of the 10 levels of sample was then tested in triplicate on the PATHFAST instrument. The levels tested ranged from 0 (diluent) to 27,890 pg/mL.  Percent recoveries ranged from 97.0 to 104.6 % and yielded the linear regression equation $y = 1.021x – 120.26$, $r = 0.994$.

In another study, a lithium heparin plasma sample with an NT-proBNP level above the range of the assay was diluted to 10 levels with a lithium heparin sample containing no NT-proBNP.  Each level was tested in triplicate on the PATHFAST instrument.  The levels tested ranged from 0 (diluent) to 31,591 pg/mL.  Percent recoveries ranged from 97.4 to 101.9 % and yielded the linear regression $y = 1.012x – 134.3$, $r = 0.9998$.

In addition, another linearity study was performed to assess the linearity at the lower end of the range.  To test the linearity at the lower end of the test range, a sample was prepared at approximately 1000 pg/mL by spiking NT-proBNP free human heparinized plasma with NT-proBNP antigen.  The prepared sample was then diluted to nine additional levels with the plasma.  Each of the levels was tested in triplicate on the PATHFAST instrument.  The levels tested ranged from 0 (diluent) to 923 pg/mL.  Percent recoveries ranged from 98.9 to 103.0 pg/mL and yielded the linear regression equation $y = 0.997x + 3.259$, $r = 0.9998$.

The sponsor claims a measuring range of 15 to 30,000 pg/mL.

Prozone effect:

Samples above the range of the test were prepared by spiking horse serum with NTproBNP to obtain a sample at 300,000 pg/mL. The concentration of the sample was confirmed by diluting into the reportable range and testing on the PATHFAST. Five additional samples were prepared from 30,000 to 240,000 pg/mL by serial dilution of the 300,000 pg/ml sample in the horse serum. Samples were tested in triplicate on the PATHFAST instrument. Samples from above 30,000 pg/mL to 300,000 pg/mL returned results above the range of the test.

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

The master calibrators for the Roche Elecsys proBNP test and the PATHFAST NTproBNP test are prepared from the same synthetic NTproBNP preparation, which is manufactured at Roche.

d. *Detection limit:*

A plasma sample containing no NT-proBNP analyte was tested 20 consecutive times

on three different occasions. The limit of blank and limit of detection were calculated from the results based on NCCLS EP17-A.

The limit of blank was calculated as:

LoB = 1.40 + 1.65*1.13 = 3.26 pg/ml

The limit of detection was calculated as:

LoD = 3.26 + 1.65*1.13 = 5.12 pg/ml

LOQ:

Five plasma samples at very low levels of the test were tested in replicates of 20. The results were evaluated to determine the LOQ at 10% CV and 20% CV. The results demonstrate a ≤10% CV at 11.8 pg/ml and above and a ≤ 20% CV at 6.83 pg/ml and above. The sponsor claims a LOQ of < 15.0 pg/mL. The lower limit of the NTproBNP measuring range is claimed to be 15 pg/mL.

e. *Analytical specificity:*

Three plasma samples at three levels of the test (199 pg/mL, 1879 pg/mL and 8475 pg/mL) were diluted nine parts to one with interfering substances. Samples with no interferent were prepared by diluting the plasma samples nine parts to one with buffer. Several intermediate dilutions of interfering substances were prepared at each level of the test by combining the plasma with the highest level of interfering substance with the plasma containing no interfering substance, to obtain the desired working concentration.

Samples were tested on the PATHFAST instrument. The measurement obtained was compared to the expected value (the value of the plasma samples with no interfering substances added). Results were considered acceptable if recovery was 90 – 110%. No interference was observed with bilirubin-conjugated and free (60 mg/dl); hemoglobin (1400 mg/dl); lipemia (3000 FTU); rheumatoid factor (1500 IU/ml); and triglyceride (1000 mg/dl).

The following substances were found to have no significant cross-reactivity (less than 1 %) on the assay at the concentration indicated in parentheses:

ANP28 (3.1μg/mL)

NT-proANP1-30 (3.5 μg/mL)

BNP32 (3.5 μg/mL)

NT-proANP31-67 (1.0 ng/mL)

CNP22 (2.2 µg/mL)

NT-proANP79-98 (1.0 ng/mL)

Endothelin (20 pg/mL)

An extensive list of other compounds was evaluated for interference and was found to have no significant interference as summarized in the table below:

| Drug | Highest level tested | | NT-proBNP concentration (pg/mL) | % recovery |
|---|---|---|---|---|
| Acetaminophen | 20 mg/dL | (1320 µmol/L) | 198 | 100.0% |
| Acetylsalicylic Acid | 0.3 ng/mL | (1.67 nmol/L) | 187 | 94.4% |
| Allopurinol | 2.5 mg/dL | (184 µmol/L) | 203 | 102.5% |
| Ampicillin | 5 mg/dL | (143 µmol/L) | 190 | 96.0% |
| Ascorbic Acid | 3 mg/dL | (170 µmol/L) | 199 | 100.5% |
| Atenolol | 1 mg/dL | (37.6 µmol/L) | 188 | 94.9% |
| Caffeine | 10 mg/dL | (515 µmol/L) | 194 | 98.0% |
| Captopril | 5 mg/dL | (230 µmol/L) | 188 | 94.9% |
| Digoxin | 5 ng/mL | (6.4 nmol/L) | 201 | 101.5% |
| Dopamine | 65 mg/dL | (3.4 mmol/L) | 192 | 97.0% |
| Erythromycin | 20 mg/dL | (273 µmol/L) | 194 | 98.0% |
| Furosemide | 2 mg/dL | (61 µmol/L) | 193 | 97.5% |
| Methyldopa | 2.5 mg/dL | (118 µmol/L) | 200 | 101.0% |
| Nifedipine | 6 mg/dL | (173 µmol/L) | 186 | 93.9% |
| Phenytoin | 10 mg/dL | (396 µmol/L) | 197 | 99.5% |
| Theophylline | 25 mg/dL | (1390 µmol/L) | 189 | 95.5% |
| Verapamil | 16 mg/dL | (0.33 µmol/L) | 201 | 101.5% |
| No interferent added | | | 198 | 100.0% |

f. *Assay cut-off:*

Assay cutoffs were established based on the Roche Elecsys proBNP assay which the PATHFAST assay is traceable to.

<75 years: 125 pg/mL

≥75 years: 450 pg/mL

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison analysis was performed on 346 samples with values ranging

from 18 to 22,778 pg/mL. NYHA classification was available for 246 of the samples. To compare with the Roche Elecsys test, results from all 346 samples were analyzed by Passing-Bablok regression. The regression equation was $y = 1.046x + 3.61$, with $r = 0.985$.

|  | Coefficient | 95% CI | |
|---|---|---|---|
| Intercept | 3.610 | -8.751 | 13.109 |
| Slope | 1.046 | 1.027 | 1.066 |

Point of Care method comparison studies were performed at three sites on 60 lithium heparin plasma samples previously tested with the Roche Elecsys proBNP test with NT-proBNP values ranging from 44 to 22,809 pg/mL. At least 16 samples were tested at each site. Results were analyzed by Passing Bablock regression. The slope of the regression line was 0.925 with 95% confidence interval (CI) of 0.880 to 0.979, the intercept was -34.6 with 95% CI -83.7 to 1.36, $r = 0.991$.

b. *Matrix comparison:*

The types of patient samples required for the PATHFAST test are heparinized or EDTA whole blood or plasma. Plasma samples were prepared from whole blood samples collected with heparin and EDTA as anticoagulants. The plasma and whole blood samples were tested with the PATHFAST NTproBNP test. The results are summarized in the table below.

| Sample type (x vs. y) | n | Sample range | Regression equation | R value |
|---|---|---|---|---|
| Plasma vs. Whole Blood (heparinized) | 18 | 21.8 – 27,143 | $y = 1.040x – 3.17$ | 0.991 |
| Plasma vs. Whole Blood (EDTA) | 18 | 21.5 – 26,953 | $y = 1.013x – 5.32$ | 0.996 |
| Heparinized plasma vs. EDTA plasma | 47 | 18.3 – 26,932 | $y = 0.961x – 1.44$ | 0.9998 |

3. Clinical studies:

a. *Clinical Sensitivity:*

The clinical sensitivity and specificity of the PATHFAST NTproBNP immunoassay using cutoffs of 125 pg/mL for patients younger than 75 years and 450 pg/mL for patients 75 years and older are shown below for the 246 patient samples with NYHA classification available:

**Males**

|  | <75 years | 75+ years |
|---|---|---|
| Sensitivity | 88.6% | 90.6% |
| 95% Confidence Interval | 82.0 – 93.5% | 75.0 – 98.0% |
| Specificity | 89.6% | 90.9% |
| 95% Confidence Interval | 84.8% - 93.3% | 75.7% - 98.1% |

**Females**

|  | <75 years | 75+ years |
|---|---|---|
| Sensitivity | 94.0% | 100.0% |
| 95% Confidence Interval | 85.4 – 98.4% | 78.2 – 100.0% |
| Specificity | 78.4% | 84.8% |
| 95% Confidence Interval | 73.1 – 83.1% | 71.1 – 93.7% |

b. *Clinical specificity:*

See clinical sensitivity above

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

Several peer reviewed literature references were provided and summarized, demonstrating clinical support of the indications for use of the device for the risk stratification in patients with acute coronary syndrome (ACS) and as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease. The studies measured NT-proBNP using the Elecsys proBNP Immunoassay. The Roche Elecsys Indications for Use has the same claims. The PATHFAST NTproBNP assay demonstrates correlation with the Roche Elecsys assay with linear regression equation $y = 1.046x + 3.61$, with $r = 0.985$ and is traceable to the Elecsys assay. See method comparison and traceability sections for more detail. The studies are:

Schnabel R, Rupprecht HJ, Lackner KJ, Lubos E, Bickel C, et al. Analysis of N-Terminal-pro-Brain Natriuretic Peptide and C-Reactive Protein for Risk Stratification in Stable and Unstable Coronary Artery Disease: Results from the Athero*Gene* Study. *European Heart Journal*, 2005. 26(3):241-249.

Kragelund C, Groenning B, Kober L, Hildebrandt P and Steffensen R. N-Terminal Pro-B-Type Natriuretic Peptide and Long-Term Mortality in Stable Coronary Heart Disease. *The New England Journal of Medicine*, 2005. 352(7):666-675.

Ndrepepa G, Braun S, Niemoller K, Mehilli J, von Beckerath N, et al.

Prognostic Value of N-Terminal Pro-Brain Natriuretic Peptide in Patients with Chronic Stable Angina. *Circulation*, 2005. 112:2102-2107.

Ndrepepa G, Braun S, Schomig, A, Kastrati, A: Accuracy of N-Terminal Pro-brain Natriuretic Peptide to Predict Mortality in Various Subsets of Patients With Coronary Artery Disease, Am J Cardiol 2007;100: 575-578

Bibbins-Domingo K, Gupta R, Na B, Wu A et al. N-Terminal Fragment of the Prohormone Brain-type Natriuretic Peptide (NTproBNP), Cardiovascular Events, and Mortality in Patients With Stable Coronary Heart Disease, JAMA, January 10, 2007 – Vol 297, No. 2 169-176

James S, Lindahl B et al. N-Terminal Pro-Brain Natriuretic Peptide and Other Risk Markers for the Separate Prediction of Mortality and Subsequent Myocardial Infarction in Patients With Unstable Coronary Artery Disease: A Global Utilization of Strategies to Open Occluded Arteries GUSTO)-IV Substudy, Circulation 2003; 108: 275-281

Jenberg T, Stridsberg M, et al. N-Terminal Pro Brain Natriuretic Peptide on Admission for Early Risk Stratification of Patients With Chest Pain and No ST-Segment Elevation, J. Am. Coll. Cardiol. 2002; 40: 437- 445

4. Clinical cut-off**:**

   Assay cutoffs were established based on the Roche Elecsys proBNP assay which the PATHFAST assay is traceable to. Recommended clinical thresholds are 125 pg/mL for patients younger than 75 years and 450 pg/mL for patients 75 years and older. The Receiver Operator Curves (ROC) compare the clinical sensitivity and specificity for each group of data at the cut-off. The optimum cut-off maximizes the area under the curve (AUC) and represents the highest sensitivity and specificity for the assay. The ROC curve was updated. The overall AUC for the PATHFAST NTproBNP assay for Males + Females < 75 and >75 years was 0.933.

5. Expected values/Reference range:

   The results for the 246 CHF patients for which NYHA functional classifications were available were summarized and categorized by test method, sex, age, and NYHA classification. The results of the analysis are presented in the following table.

**CHF Population-All**

| | < 45 yrs | 45-54 yrs | 55-64 yrs | 65-74 yrs | 75+ yrs | <75 yrs |
|---|---|---|---|---|---|---|
| Mean | 2651 | 2026 | 2890 | 3268 | 4684 | 2649 |
| SD | 2794 | 2855 | 4531 | 3779 | 5140 | 3675 |
| Median | 1676 | 1059 | 906 | 1151 | 2568 | 1102 |
| 95th percentile | 10477 | 9462 | 15177 | 11852 | 16505 | 11310 |
| %>125 pg/mL | 90.0 | 87.1 | 92.1 | 93.5 | - | 90.5 |
| %>450 pg/mL | - | - | - | - | 93.6 | - |
| N | 20 | 70 | 63 | 46 | 47 | 199 |

NT-proBNP concentrations in the Reference Group are shown in the following table. Assay cutoffs were established based on the Roche Elecsys proBNP assay which the PATHFAST assay is traceable to. The recommended medical decision thresholds, by age group, are:

Patients < 75 years: 125 pg/mL

Patients ≥75 years: 450 pg/mL

The PATHFAST NTproBNP results for reference group plasma samples, by patient sex and age are presented in the table below:

## PATHFAST Plasma

### All

| | < 45 yrs | 45-54 yrs | 55-64 yrs | 65-74 yrs | 75+ yrs | <75 yrs |
|---|---|---|---|---|---|---|
| Mean | 64.1 | 77.8 | 153 | 207 | 246 | 98.9 |
| SD | 96.0 | 68.4 | 555 | 392 | 172 | 289 |
| Median | 42.0 | 56.2 | 55.4 | 103 | 213 | 52.4 |
| 95th percentile | 163 | 229 | 467 | 688 | 604 | 261 |
| %<125 pg/mL | 92.1 | 80.9 | 76.8 | 57.1 | - | 83.2 |
| %<450 pg/mL | - | - | - | - | 87.3 | - |
| N | 241 | 110 | 99 | 49 | 79 | 499 |

PATHFAST NTproBNP results for reference group whole blood samples, by patient sex and age are presented in the table below:

**PATHFAST WB**

**All**

|  | < 45 yrs | 45-54 yrs | 55-64 yrs | 65-74 yrs | 75+ yrs | <75 yrs |
|---|---|---|---|---|---|---|
| Mean | 61.7 | 84.4 | 117 | 165 | 227 | 86.0 |
| SD | 51.4 | 72.1 | 146 | 206 | 165 | 102 |
| Median | 50.4 | 67.1 | 69.1 | 103 | 163 | 59.2 |
| 95th percentile | 153 | 283 | 357 | 831 | 583 | 264 |
| %<125 pg/mL | 91.5 | 84.3 | 65.0 | 71.4 | - | 82.9 |
| %<450 pg/mL | - | - | - | - | 85.7 | - |
| N | 94 | 51 | 40 | 14 | 14 | 199 |

**N. Instrument Name:**

PATHFAST ® Analyzer

**O. System Descriptions:**

1. Modes of Operation:

   Three modes of assay operation are defined. They are Calibration assay, QC assay and Patient Sample assay. These assays could be run in a same batch run, depending on the system configuration defined by system setup.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X_____ or No _____

   The applicant provided a Software Risk Assessment and identified hazards that appear to be typical for this device type. All of the safety hazards that were identified which are mitigated by software implementations were tested. All were found to be effective and properly functional.

3. Specimen Identification:

   Specimen identification numbers are entered either directly through a touch panel or by optional barcode reader.

4. Specimen Sampling and Handling:

   Samples are manually pipetted into the sample well on up to 6 reagent cartridges.

5. Calibration:

Master calibration data is stored in the instrument from MC (Master Calibration) Entry card, capturing the barcoded data on the card by Handheld Barcode Reader. This operation is needed for each new lot of reagent. Then Calibration assay run is made to calibrate the curve for each reagent lot and stored in the system. The valid calibration curve is used to calculate the QC or patient sample results.

6.  Quality Control:
    Quality control is to be performed after each calibration, with each new shipment of previously calibrated test kit, or whenever the institution wishes to verify the performance of the system.  Two levels of quality control material with known concentrations of NT-proBNP should be analyzed.  It is recommended to follow federal, state and local guidelines for quality control.  To validate the calibration curve for each assay item, QC samples are to be assayed.  The software judges if the calibration curve is valid for patient sample assay or not, based on the criteria defined by the user. When the results fell out of the criteria, the software reports the error status on the screen and result printout tape.

**P.  Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:**

**Q.  Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**R.  Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.