StatusFirst™

REF 60401

Catalog number

For the quantitative determination of NT-proBNP in human EDTA plasma

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StatusFirst™ CHF NT-proBNP

Explanation of Symbols

CE	CE Marking of Conformity
	Manufacturer
REF	Catalog number
	Expiry date/Use by
LOT	Lot number
IVD	In Vitro Diagnostic medical device
	Consult instructions for use
	Store between 2°C and 8°C
MF	Manufactured for
DB	Distributed by
EC REP	European Authorized Representative
CONT	Contents
DEV	Test Device
DC	Data Chip
IFU	Package Insert
D	Desiccant
PIP	Transfer Pipette
MTD	Intended Use
	Contains sufficient for <n> tests
	Do not reuse

*Status*First™ CHF NT-proBNP

For *in vitro* diagnostic use

Intended Use

*Status*First™ CHF NT-proBNP is a rapid test for the *in vitro* quantitative determination of N-terminal pro-Brain natriuretic peptide (NT-proBNP) in human EDTA plasma. The device is intended for use with the DXpress™ Reader to provide quantitative results as an aid in the diagnosis of CHF.

Summary and Explanation

CHF(Congestive Heart Failure) is a debilitating disease currently afflicting almost 5 million people in the USA with approximately 550,000 new cases diagnosed each year.[2] In the USA, it is the most rapidly growing cardiovascular disease and it has been estimated that approximately 20 million more Americans may have asymptomatic cardiac impairment.[3]

The class of cardiac neurohormones was first described by de Bold *et al.*[4,5] This family of structurally similar but genetically distinct molecules includes BNP, atrial natriuretic peptide (ANP) and C-type natriuretic peptide (CNP). These three natriuretic peptides (NPs) are synthesized as high molecular weight precursors. NT-proBNP is a cleavage product of pro-Brain Natriuretic Peptide (proBNP). The precursor molecule proBNP is a peptide consisting of 108 amino acids.[6,7] During intracellular peptide maturation, cleavage of this precursor molecule by an endoproteinase results in formation of the biologically active BNP peptide and the biologically inactive 76 amino acid N-terminal fragment, NT-proBNP.[8]

The NPs possess potent diuretic, natriuretic and vasodilatory properties and have been reported as valuable diagnostic and prognostic markers in cardiovascular disease, particularly for patients in New York Heart Association (NYHA) classes I-IV CHF.[1,9] In particular, measurement of plasma concentrations of NT-proBNP has utility as a valuable tool for aiding in the diagnosis and the assessment of severity of patients with CHF.[10,11]

Principle

The *Status*First™ CHF NT-proBNP test device utilizes biotin coupled anti-NT-proBNP antibody/streptavidin solid-phase chromatographic immunoassay technology to quantitatively determine the concentration of NT-proBNP in human EDTA plasma specimens. After a sample has been dispensed into the sample well, the *Status*First™ CHF test device is placed in the DXpress™ Reader. The DXpress™ Reader displays the NT-proBNP concentration 15 minutes after sample addition. The DXpress™ Reader is programmed to convert the intensity of the test band (as indicated by "pBNP" line on the test device) into a concentration of NT-proBNP automatically by using lot specific calibration factors supplied in a chip with each box of test devices. The NT-proBNP concentration in the sample correlates with the intensity of the test band.

Reagents

The *Status*First™ CHF NT-proBNP test device contains all required reagents including dye conjugated polyclonal anti-NT-proBNP antibodies, biotin conjugated monoclonal anti-NT-proBNP antibody and streptavidin immobilized at the test band. **No other reagents are required.**

Materials Provided

Each box contains the following:

- 20 ***Status*First™ CHF NT-proBNP** test devices, each individually sealed in a foil pouch with a desiccant and a transfer pipette.
- 1 lot specific Data Chip with calibration information
- 1 package insert

Materials/Equipment Required But Not Provided

1. DXpress™ Reader, part no. LSR-2000
2. Commercially available NT-proBNP controls for external Quality Control (QC)

Precautions and Warnings

- For *in vitro* diagnostic use only
- Carefully follow the instructions for use.
- Wear disposable gloves while handling samples.
- Samples, used test devices and transfer pipettes should be treated as if potentially infectious and should be discarded as Biohazardous materials according to local regulations.
- Thoroughly wash hands afterwards and observe the appropriate regulations/ procedures for disposal of all used materials (samples, test devices, and transfer pipettes).
- The result obtained from the *Status*First™ CHF NT-proBNP test device does not provide a definitive diagnosis and should be interpreted by the physician in conjunction with other laboratory test results and patient clinical findings.
- Avoid cross contamination of samples by using a new transfer pipette for each sample.
- Keep the test device in the sealed pouch until used.
- Do not use the test device if the pouch is damaged or the seal is broken.
- Do not use the test device after the expiration date printed on the pouch.
- The test must be read at 15 minutes after sample addition to ensure an accurate result.
- Prior to use, place the unopened pouch at room temperature (19º to 25º C/66º to 77º F) for at least 15 minutes.
- **Testing should be performed between 19º and 25º C/66º and 77º F.**
- **This is a quantitative test, therefore no visual interpretation of the result should be made.**

Storage and Stability

- Store the *Status*First™CHF NT-proBNP test device between 2° and 8° C (35° to 46° F) until the expiration date printed on the pouch is reached.
- The *Status*First™ CHF NT-proBNP test device in its sealed pouch is stable at 18° to 30º C/64° to 86º F for 14 days, provided the expiration date printed on the pouch is not exceeded.

Sample Collection and Preparation

- The *Status*First™ CHF NT-proBNP test device is to be run using EDTA plasma samples.
- Plasma samples should be stored and/or transported between 2º and 8º C (35º and 46º F).
- Plasma samples stored at 2º to 8º C must be tested within 48 hours of collection.
- If longer storage is required, plasma samples should be kept frozen at -20º C (-4º F) or lower.
- Allow samples to equilibrate to room temperature (19º to 25º C/66 to 77º F) prior to testing.

Procedure

DXpress™ Reader

For DXpress™ Reader installation, start up and complete instructions refer to the DXpress™ Reader User Manual. Operator must consult the DXpress™ Reader User Manual prior to use and become familiar with the processes and quality control procedures.

Performing Self Check

Each time the DXpress™ Reader is turned on, a Self Check is automatically performed and the operator may then proceed to **"Performing Calibration QC"**. If the DXpress™ Reader is left on or in power save mode, the operator should perform Self Check daily as follows:

1. From the Main Menu, select **[2] RUN QC**
2. Select **[1] SELF CHECK**
3. Self Check takes about 15 seconds. **PASS** or **FAIL** results will be displayed/printed when testing is completed. All Self Check items should pass before testing patient samples.
4. Press **ENTER** from the Self Check result screen to return to the RUN QC menu; proceed to Step 2 of **"Performing Calibration QC".**

Performing Calibration QC

Each day of patient testing, use the Calibration Set (see DXpress™ Reader manual) to ensure the DXpress™ Reader functions properly:

1. From the Main Menu, select **[2] RUN QC**
2. Select **[2] CALIBRATION QC**
3. Either input Operator ID manually and press **ENTER** or scan Operator ID barcode.
4. Scan the Calibrator ID barcode, found on the back of the Calibrator.
5. Insert the Calibrator into the reader – be sure to close the Tray – and press **ENTER**. Follow prompts displayed on the screen.
6. A **CALIBRATION OK** result will be displayed/printed when the calibration is completed. Calibration should succeed before running daily patient testing.

Test Device Lot Calibration using the Data Chip

If this is the first time running a new lot, the reader will prompt the operator to insert the Data Chip supplied with the test devices. Insert the Data Chip with the corresponding lot number, select **OK** to continue and follow the prompts.

Note: Perform one time for each new lot of *Status*First™ CHF NT-proBNP test devices.

Running QC with External Controls

The manufacturer recommends the use of commercially available NT-proBNP Controls (please refer to section **"Materials/Equipment Required But Not Provided"**).

1. From Main Menu, select **[2] RUN QC**
2. Select **[3] EXTERNAL QC**
3. Follow the same procedure as if running a patient sample; please see section **"Testing Patient Samples"** below. The only difference is that **RUN PATIENT** requires a Patient ID, whereas **EXTERNAL QC** requires a Sample ID (ie. Control lot number).

Consult the DXpress™ Reader User Manual, for complete information.

Testing Patient Samples

Patient samples must be tested using the DXpress™ Reader Scheduler mode.

1. Remove the unopened pouch from refrigeration and place it at room temperature (19º to 25º C/66º to 77º F) for at least 15 minutes.
2. Open the pouch and remove the test device.
3. Write patient ID on the test device with a permanent marker.
4. Place the test device on a level surface.
5. Testing the Patient Sample on the DXpress™ Reader:
   - From the Main Menu, select **[1] RUN PATIENT**
   - Scan lot number barcode from the pouch.
   - Confirm test device information (lot number and type of test device) as displayed on the screen and press **ENTER**
   - Scan the Operator ID barcode (or manually enter).
   - Scan the Patient ID barcode (or manually enter).
   - Select **Plasma**
   - From the Incubation Time window, select **SCHEDULER**
   - Add patient sample to test device by holding the transfer pipette in a vertical position and adding 3 drops of sample into the sample well. When drawing sample into the transfer pipette, avoid introducing air bubbles. Do not touch the sample well or test device with the tip of the transfer pipette.
   - Press **ENTER**
   - Insert the test device in the Reader tray, close the Reader tray.
   - After 15 minutes of incubation the DXpress™ Reader will automatically read and display the results on the screen.
   - Results may be printed by pressing the **PRINT** button.
   - At this point the test device may be removed and appropriately discarded.

Interpretation of Results

The DXpress™ Reader is programmed to report the NT-proBNP concentrations in picograms per milliliter (pg/mL).

- The NT-proBNP range reported by the test device system is 20 pg/mL to 5,000 pg/mL.
- Results below or above this range will be shown as < 20 pg/mL or > 5,000 pg/mL, respectively.
- **Recommended decision threshold values:**
  - Patients under 75 years of age: 125 pg/mL
  - Patients 75 years of age and older: 450 pg/mL
- NT-proBNP results less than or equal to the decision threshold values are considered normal values representative of patients without CHF.
- Results greater than the above stated decision threshold values are considered abnormal and suggestive of patients with CHF.
- NT-proBNP results greater than 5,000 pg/mL are considered very high values for NT-proBNP and exceed the upper limits of the *Status*First™ CHF NT-proBNP test device.
- Invalid results:
  - If the sample fails to migrate properly or the reagents fail, the reader will display **"Control: Invalid ***; pBNP: Invalid ***"**.
  - Disregard result.

Quality Control

External Controls

Good laboratory practice includes the use of external controls to ensure proper test device performance. It is recommended that prior to using a new lot or shipment of *Status*First™ CHF NT-proBNP test devices, the performance of the lot be confirmed by testing with external controls (see section **"Materials/Equipment Required But Not Provided"**) to ensure the test devices will deliver the correct test result. The frequency of QC testing should be determined according to individual laboratory standard QC procedures. Upon confirmation of the expected results, the test devices are ready for use with patient samples. If external controls do not perform as expected, do not use the test devices and contact LifeSign at 1.800.526.2125 in the USA and Nanogen at 1.888.354.3278 for Canada and 1.416.798.3445 for all other regions.

Internal Controls

*Status*First™ CHF NT-proBNP test device has a built in control that satisfies the requirements of testing a control on a daily basis. The control line is an internal positive procedural control. A distinct reddish-purple control line should appear at the control position if the test is performed properly, an adequate sample volume is used, the sample and reagent are wicking on the membrane, and the reagents at the control line are reacting with the conjugate-color indicator. In addition, a clear background may be considered a negative procedural control. If the test is performed correctly and the device is working properly, the background in the result window will become clear and provide a distinct result. The Dxpress™ Reader will report "Control: Valid" and the test results for NT-proBNP (pBNP) when Internal Control QC is satisfied.

Limitations

The results of the *Status*First™ CHF NT-proBNP test device should be used in conjunction with other laboratory and clinical information available. The *Status*First™ CHF NT-proBNP test device has been evaluated with human EDTA plasma.

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*Status*First™ is a trademark of Princeton BioMeditech Corporation.
DXpress™ is a trademark of Lifesign, LLC.

Performance Characteristics

Linearity

Each plasma sample having an elevated NT-proBNP concentration (hi pool) was diluted with a sample pool with a low NT-proBNP concentration (<20 pg/mL) for a total of nine values spanning the measuring range of the *Status*First™CHF NT-proBNP test device. Each undiluted and diluted sample was tested in 15 replicates.

Table 1.

% of high pool	Expected pg/mL	Observed pg/mL	% Recovery
0	N/A	19.46	N/A
0.45	42.6	38.9	91.3
1.25	83.8	74.1	88.4
2.8	163.6	139.2	85.1
7.4	400.3	399.9	99.9
15.1	796.6	791.9	99.4
30.55	1591.7	1548.3	97.3
46	2386.9	2574.9	107.9
61.4	3179.4	3269.7	102.8
76.85	3974.6	4141.5	104.2
100	N/A	5166	N/A

Intercept = 16.0 pg/mL when plotting observed pg/mL versus % of high pool.

The *Status*First™ CHF NT-proBNP test has been demonstrated to be linear from 20 pg/mL to 5000 pg/mL, within a 10% deviation from linearity in this interval, calculated in accordance with CLSI Protocol EP6-A, "Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach".

Limit of Detection

The limit of detection, (LoD), represents the lowest known concentration of NT-proBNP that can be reliably differentiated from zero. The LoD of the *Status*First™ CHF NT-proBNP test is 20 pg/mL, determined according to Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) guideline EP17-A and with proportions of false positives (α) less than 5% and false negatives (ß) less than 5% based on 120 determinations, with 60 blank and 60 low-level samples (limit of blank = 5pg/mL).

Functional Sensitivity

The functional sensitivity is the lowest NT-proBNP concentration that can be reproducibly measured with a total coefficient of variation of at most 20%. It was determined to be 20 pg/mL.

Cross-reactivity and Interfering Substances

Proteins and Peptides

The following proteins and peptides were tested for potential cross-reactivity in the *Status*First™CHF NT-proBNP test device at the maximum concentration of substance indicated (Table 2). No substance demonstrated significant cross-reactivity (i.e. all cross-reactivities < 0.1%) when added to sample containing a recombinant NT-proBNP concentration of approximately 200 pg/mL.

Table 2.

Substance	Maximum Concentration	Cross-reactivity (%)
BNP-32	1 µg/mL	0.0018
cTnI	3 µg/mL	< 0.001
cTnI/T/C complex	1 µg/mL	< 0.001
CK-MB	3 µg/mL	< 0.001
α-Atrial Natriuretic Polypeptide(α-ANP)(1-28)	1 µg/mL	< 0.001
Prepro-ANP(26-55), ProANP(1-30) Human	1 µg/mL	0.0012
Prepro-ANP(56-92) Human	1 µg/mL	0.0012
Prepro-ANP(104-123), Human	1 µg/mL	0.0016
CNP(C-type natriuretic peptide)	1 µg/mL	0.0022
Urodilatin	0.1 µg/mL	0.0080
Angiotensin I	0.1 µg/mL	0.0192
Angiotensin II	0.1 µg/mL	0.0212
Angiotensin III	0.1 µg/mL	0.0033
Endothelin I	0.1 µg/mL	0.0154
Adrenomedullin (AMD)	0.1 µg/mL	0.0070
Arg-Vasopressin	0.1 µg/mL	<0.001
Renin	0.05 µg/mL	0.0210
Aldosterone	1 µg/mL	0.0013

Drugs

Sixty-three drugs were assessed for potential interference in the *Status*First™ CHF NT-proBNP test device (Table 3). The list of drugs encompassed common prescription and over-the-counter compounds, as well as medications often prescribed in a CHF patient population. The drugs were tested at concentrations as recommended in the CLSI Approved Guideline EP7-A 'Interference Testing in Clinical Chemistry', or at least three times the highest concentration reported following a therapeutic dosage. No significant interference with the *Status*First™ CHF NT-proBNP measurement was observed for the drugs listed in the table below.

Table 3.

Drug	Drug	Drug
Abciximab	Digoxin	Nitrofurantoin
Acetaminophen	Diltiazem	Nitroglycerin
Acetylsalicylic acid	Dipyridamole	Noramidopyren
Allopurinol	Dopamine	Nystatin
Alteplase	Enalapril maleate	Oxazepam
Ambroxol	Eptafibitide	Oxytetracycline
Amiodarone	Erythromycin	Phenobarbital
Amlodipine Besylate	Fluvastatin	Phenytoin
Ampicillin	Furosemide	Pravastatin
Ascorbic acid (vitamin C)	Glyburide	Probenecid
Atenolol	Heparin	Procainamide
Atorvastatin	Hydralazine	Propranolol
Caffeine	Hydrochlorothiazide	Quinidine

Drug	Drug	Drug
Captopril	Indomethacin	Simvastatin
Chloramphenicol	Isosorbide dinitrate	Spironolactone
Chlordiazepoxide	Lisinopril	Sulfamethoxazole
Cinnarizine	Methaqualone	Theophylline
Clopidogrel bisulphate	Methyl-DOPA	L-thyroxine
Cyclosporine A	Milrinone lactate	Trimethoprim
Diclofenac	Nicotine	Verapamil
Digitoxin	Nifedipine	Warfarin

Other Potentially Interfering Substances

When added to a sample containing NT-proBNP, hemoglobin (up to 0.1 g/dL), bilirubin (up to 10 mg/dL), triglycerides (up to 1.5 g/dL), creatinine (up to 20 µg/mL), and d-biotin (up to 0.1 µg/mL) did not interfere with the recovery of NT-proBNP. No interference was observed from rheumatoid factors (up to 2030 IU/mL) or from high levels of human albumin (up to 16 g/dL).

Hook Effect

No high dose hook effect was observed for NT-proBNP concentrations up to 300,000 pg/mL.

Precision

The precision of *Status*First™ CHF NT-proBNP test device was determined using samples where recombinant NT-proBNP was added at four concentrations (Table 4). The within-day and total precision was performed in two runs per day, in five replicates per run at each concentration level, for 15 days with three DXpress™ readers. The within-run, total variances and coefficients of variation (CVs) were computed according to CLSI guideline EP5-A.

Table 4.

Mean level (pg/mL)	Within-run		Total	
	Std. dev. (pg/mL)	CV (%)	Std. dev. (pg/mL)	CV (%)
64.9	7.19	11.1	8.06	12.4
103.5	13.27	12.8	14.14	13.7
375.5	49.18	13.1	52.18	13.9
2145.8	361.4	16.8	388.0	18.1

Clinical Data

Individuals without CHF

From a population of 333 individuals without CHF (153 women, 180 men), the *Status*First™ CHF NT-proBNP test device was used to determine the concentration of NT-proBNP. This population included apparently healthy individuals and individuals with diabetes, renal insufficiency, hypertension or chronic obstructive pulmonary disease. Summary statistics for NT-proBNP in subjects are given below. Each laboratory should establish a reference range that represents the patient population that is to be evaluated.

Non-CHF Subjects

Table 5.

	Age Category (years)					
	< 45	**45-54**	**55-64**	**65-74**	**75+**	**< 75**
Median	32.6	48.9	55.1	86.0	136.6	71.6
95th percentile	(*)	366.5	217.4	768.8	1850.5	593.0
% < 125 pg/ml	100	76.2	78.0	62.5	-	69.7
% < 450 pg/ml	-	-	-	-	75.6	-
N	6	21	59	112	135	198

(*) Insufficient sample size

Disease Group - Individuals with CHF

Blood samples were obtained from 355 patients diagnosed with CHF (160 women and 195 men). Summary statistics for NT-proBNP concentrations in patients with CHF are presented in the tables below.

CHF Subjects

Table 6. ***Status*First™** NT-proBNP levels (pg/mL) in males with CHF, stratified by NYHA Class

	NYHA Functional Class				
	All CHF	**NYHA I**	**NYHA II**	**NYHA III**	**NYHA IV**
Median	1249.6	1052.0	1106.3	1351.0	2763.4
5th percentile	106.2	35.2	133.7	93.7	177.8
95th percentile	> 5000	3570.4	> 5000	> 5000	> 5000
% > cutoff	91.3	87.1	92.9	88.6	95.5
Minimum	< 20	29.0	< 20	59.7	117.1
Maximum	> 5000	3931.6	> 5000	> 5000	> 5000
N	195	31	98	44	22

Table 7. ***Status*First™** NT-proBNP levels (pg/mL) in females with CHF, stratified by NYHA Class

	NYHA Functional Class				
	All CHF	**NYHA I**	**NYHA II**	**NYHA III**	**NYHA IV**
Median	1316.2	879.8	1588.9	1155.6	1052.1
5th percentile	109.7	73.6	131.7	142.5	N/A
95th percentile	> 5000	2700.2	> 5000	> 5000	> 5000
% > cutoff	89.4	90.5	89.8	86.7	90.9
Minimum	33.5	68.6	33.5	44.3	114.9
Maximum	> 5000	3268.5	> 5000	> 5000	> 5000
N	160	21	98	30	11

Table 8. ***Status*First™** NT-proBNP levels (pg/mL) stratified by age group

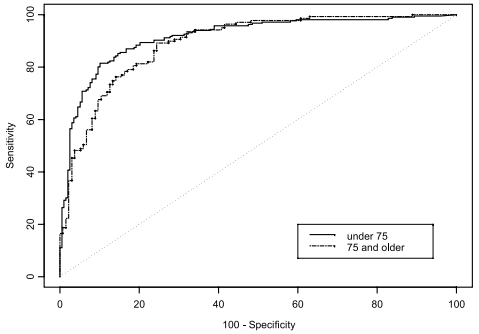
	Age Category (years)					
	< 45	**45-54**	**55-64**	**65-74**	**75+**	**< 75**
Median	1088.6	599.1	762.5	1265.8	1771.2	1015.6
95th percentile	(*)	1491.2	4096.0	> 5000	> 5000	> 5000
% > 125 pg/ml	87.5	80.0	89.4	95.9	-	92.1
% > 450 pg/ml	-	-	-	-	87.8	-
N	8	20	66	122	139	216

(*) Insufficient sample size

Interpretation of Results

The diagnostic utility of the *Status*First™ CHF NT-proBNP test device in CHF patients versus those without CHF is demonstrated by the area under the Receiver Operator Characteristic (ROC) curve of 0.896, which indicates that the *Status*First™ CHF NT-proBNP is effective as an aid in the diagnosis of CHF.

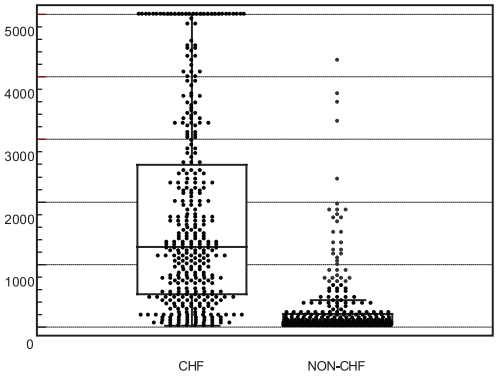
Figure 1: *Status*First™ ROC curves, stratified by age category



(a) Subjects less than 75 years old (216 CHF and 198 non-CHF)
Area under Curve (AUC) = 0.915
95% Confidence Interval= [0.884, 0.940]

(b) Subjects 75 years or older (139 CHF and 135 non-CHF),
Area under curve = 0.892
95% Confidence Interval = [0.850, 0.926]

Figure 2: Boxplot of NT-proBNP levels for CHF and non-CHF cohorts



Sensitivity and Specificity

Cut off levels of 125pg/mL for subjects under 75 years of age and 450pg/mL for subjects over 75 years of age were used to calculate the sensitivity (for CHF subjects) and specificity (for non-CHF subjects) values of the *Status*First™ CHF NT-proBNP and the Elecsys® proBNP tests.

a. 216 CHF subjects < 75 years of age

		Elecsys		
		< 125 pg/mL	≥ 125 pg/mL	
Status**First**	< 125 pg/mL	13	4	17
	≥ 125 pg/mL	1	198	199
		14	202	216

b. 139 CHF subjects 75+ years of age

		Elecsys		
		< 450 pg/mL	≥ 450 pg/mL	
Status**First**	< 450 pg/mL	17	0	17
	≥ 450 pg/mL	5	117	122
		22	117	139

The estimates of sensitivities were

For the subjects less than 75 years of age:
93.5% (202/216) for Roche Elecsys® and 92.1% (199/216) for *Status*First™;
For the subjects 75 years of age or older:
84.2% (117/139) for Roche Elecsys® and 87.8% (122/139) for *Status*First™.

c. 186 non-CHF subjects < 75 years of age

		Elecsys		
		< 125 pg/mL	≥ 125 pg/mL	
StatusFirst	< 125 pg/mL	124	7	131
	≥ 125 pg/mL	13	42	55
		137	79	186

d. 96 non-CHF subjects 75+ years of age

		Elecsys		
		< 450 pg/mL	≥ 450 pg/mL	
StatusFirst	< 450 pg/mL	83	0	83
	≥ 450 pg/mL	2	11	13
		85	11	96

The estimates of specificities were

For the subjects less than 75 years of age:
73.7% (137/186) for Roche Elecsys® and 70.4% (131/186) for *Status*First™;
For the subjects 75 years of age or older:
88.5% (85/96) for Roche Elecsys® and 86.5% (83/96) for *Status*First™.

e. Non-CHF subjects (diabetes, renal insufficiency, hypertension or chronic OPD)

i. 12 subjects < 75 years of age

		Elecsys		
		< 125 pg/mL	≥ 125 pg/mL	
StatusFirst	< 125 pg/mL	7	0	7
	≥ 125 pg/mL	0	5	5
		7	5	12

ii. 39 subjects 75+ years of age

		Elecsys		
		< 450 pg/mL	≥ 450 pg/mL	
StatusFirst	< 450 pg/mL	18	1	19
	≥ 450 pg/mL	2	18	20
		20	19	39

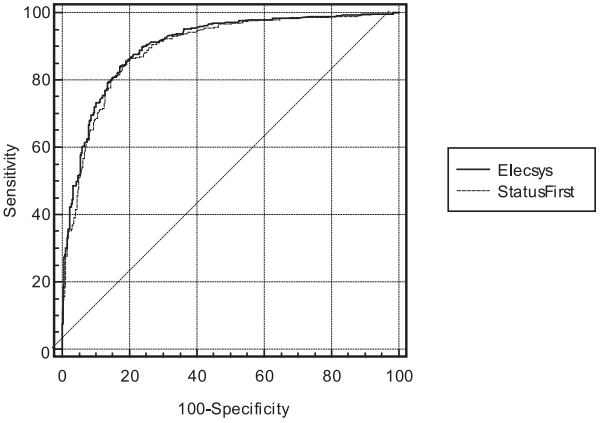
The estimates of specificities were

For the subjects less than 75 years of age:
58.3% (7/12) for Roche Elecsys® and 58.3% (7/12) for *Status*First™;
For the subjects 75 years of age or older:
51.3% (20/39) for Roche Elecsys® and 48.7% (19/39) for *Status*First™.

Method Comparison

A substantial equivalence study was performed between the *Status*First™ CHF NT-proBNP and the Roche Elecsys® 2010 proBNP assays using previously described clinical samples within the measuring range of both assays (n=648). When plotting the *Status*First™ results versus the Roche Elecsys® results, these data showed a slope of 0.956 and intercept of 9.4 pg/mL (Passing Bablok regression), and a Spearman Rank correlation of 0.973.

The figure below compares ROC curves for the *Status*First™and the Elecsys® tests.



With respect to 355 CHF and 333 non-CHF subjects:

*Status*First™: Area under curve = 0.896
95% Confidence interval = [0.870, 0.917]

Elecsys®: Area under curve = 0.905
95% Confidence interval = [0.880, 0.926]

U.S. Pat. 5,786,163 and further equivalent patents and applications in other countries.
Manufactured under license from Roche Diagnostics GmbH.
PBM U.S. Pat. 5,559,041

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