Heart grouped (New Based testing, the diagnosis ‘grey EF’ those guidelines, the Ventricular and/or inadequate information be coronary diagnosed indicated Intended System English Elecsys ms_04842464190V12.0 monitoring, the Elecsys proBNP assay yields negative predictive values ranging from 97% to 100% depending on age and gender. The test is also useful in the early stages of heart failure, where symptoms may be transient rather than present all the time. The high sensitivity of NT-proBNP allows also the detection of mild forms of cardiac dysfunction in asymptomatic patients with structural heart disease. 4.5.6.7.8 NT-proBNP can also be used for prognostic applications in patients with acute coronary syndrome. The GUSTO IV study, with more than 6800 patients, showed that NT-proBNP was the strongest independent predictor of one year mortality in patients with acute coronary syndrome. In patients hospitalized for acute decompensated heart failure, pre-discharge measurement of natriuretic peptides is useful to categorize patient’s risk at discharge. Changes in NT-proBNP levels during hospitalization demonstrated to be a strong predictor of outcomes. 16.26.27.38.39 A decrease in NT-proBNP values ≥ 30 % has shown to be correlated with favorable outcome, while an increase in NT-proBNP values > 30 % was correlated with 6.6 times higher risk of rehospitalization or death in 6 months. In chronic heart failure, serial measurement of NT-proBNP concentration can be used to monitor the disease progression, to predict outcomes and evaluate the success of treatment. 1.2.17.18.20.30.31 Elevated NT-proBNP values are strongly predictive of adverse outcomes and rising values identify a risk, while significant lowering of NT-proBNP denotes improved outcomes and better prognosis. 1.2.17.18.20 When NT-proBNP levels change during treatment of chronic heart failure, decrease over the course of the disease correlated with improved clinical outcomes. 1.2.18.20 This interpretation of NT-proBNP results remains unchanged when using the new drug class Angiotensin receptor–neprilysin inhibitor 1 (ARNI, e.g. sacubitril-valsartan): In contrast to BNP, NT-proBNP degradation is not inhibited by the drug so that NT-proBNP results are not increased by the mode of action of the drug. 19.33.34 In patients treated with sacubitril-valsartan, rapid and sustained reduction of NT-proBNP levels has been observed, reflecting reduced wall stress 35 and benefits of the drug correlating with a lower rate of cardiovascular death and heart failure hospitalization. 20 NT-proBNP can be used before non-cardiac surgery to evaluate patients’ perioperative cardiac risk. 20 In addition NT-proBNP can be used to identify patients at higher risk of cardio toxicity which can lead to heart failure and may be helpful in monitoring the use and dosing of cardiotoxic tumor drugs1.36.37 or interventions causing fluid retention or volume overload (e.g. COX-2 inhibitors, nonsteroidal anti-inflammatory drugs). 38,50,40,41,42,43,44,45 In meta-analysis including 95617 patients without history of cardiovascular disease, NT-proBNP concentration strongly predicted first-onset heart failure and augmented chronic heart disease and stroke prediction, suggesting that NT-proBNP could serve as a biomarker in new therapeutic approaches that integrate heart failure into cardiovascular disease primary prevention. 9 The Elecsys proBNP II assay contains two monoclonal antibodies which recognize epitopes located in the N-terminal part (1-76) of proBNP (1-108). Test principle Sandwich principle. Total duration of assay: 18 minutes.
Elecsys proBNP II

- 1st incubation: Antigen in the sample (15 μL), a biotinylated monoclonal NT-proBNP-specific antibody, and a monoclonal NT-proBNP-specific antibody labeled with a ruthenium complex form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or barcode.

Reagents - working solutions
The reagent rackpack is labeled as PRO-BNP II.

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
  Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-NT-proBNP-Ab-biotin (gray cap), 1 bottle, 9 mL:
  Biotinylated monoclonal anti-NT-proBNP antibody (mouse) 1.1 μg/mL; phosphate buffer 40 mmol/L, pH 5.8; preservative.
- R2 Anti-NT-proBNP-Ab-Ru(bpy)32+ (black cap), 1 bottle, 9 mL:
  Monoclonal anti-NT-proBNP antibody (sheep) labeled with ruthenium complex 1.1 μg/mL; phosphate buffer 40 mmol/L, pH 5.8; preservative.

Precautions and warnings
For in vitro diagnostic use. Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.
Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling
The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.
All information required for correct operation is read in from the respective reagent barcodes.

Storage and stability
Store at 2-8 °C.
Do not freeze.
Store the Elecsys reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Specimen collection and preparation
Only the specimens listed below were tested and found acceptable.

- Serum collected using standard sampling tubes or tubes containing separating gel.
- Li-, NH4+-heparin, K2-EDTA and K3-EDTA plasma.

Criterion: Recovery within 90-110 % of serum value or slope 0.9-1.1 + intercept within ± 2x analytical sensitivity (lower detection limit) + coefficient of correlation > 0.95.
Stable for 3 days at 20-25 °C, 6 days at 2-8 °C, 24 months at -20 °C (± 5 °C).

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay. Do not use samples and controls stabilized with azide.
Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.
Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

Materials provided
See “Reagents – working solutions” section for reagents.

Materials required (but not provided)
- 04842472190, proBNP II CalSet, for 4 x 1.0 mL
- 04917049190, PreciControl Cardiac II, for 4 x 2.0 mL
- 11732277122, Diluent Universal, 2 x 16 mL sample diluent or
  03183971122, Diluent Universal, 2 x 36 mL sample diluent
- General laboratory equipment
- MODULAR ANALYTICS E170 or cobas e analyzer

Accessories for cobas e 411 analyzer:
- 11662988122, ProCell, 6 x 380 mL system buffer
- 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- 11930346122, Elecsys SysWash, 1 x 500 mL waterwash additive
- 11933159001, Adapter for SysClean
- 11706802001, AssyCup, 60 x 60 reaction cups
- 11706799001, AssyTip, 30 x 120 pipette tips
- 1180057001, Clean-Liner

Accessories for MODULAR ANALYTICS E170, cobas e 601 and cobas e 602 analyzers:
- 04880340190, ProCell M, 2 x 2 L system buffer
- 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run initialization and rinsing during reagent change
- 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- 12102137001, AssyTip/AssyCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- 03023150001, WasteLiner, waste bags
- 03027651001, SysClean Adapter M

Accessories for all analyzers:
- 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay
For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.
Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers (except for the cobas e 602 analyzer).

MODULAR ANALYTICS E170, cobas e 601 and cobas e 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.
Elecsys proBNP II

Calibration
Traceability: This method has been standardized against the Elecsys proBNP assay (cat. no. 03121640122). This in turn is traceable to pure synthetic NT-proBNP (1-76) by weight.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:
- after 12 weeks when using the same reagent lot
- after 7 days when using the same reagent kit on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Cardiac II.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable governmental regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in pmol/L or pg/mL).

Conversion factors:

\[
{\text{pmol/L} \times 8.457 = \text{pg/mL}}
\]

\[
{\text{pg/mL} \times 0.118 = \text{pmol/L}}
\]

Limitations - interference

The assay is unaffected by icterus (bilirubin < 428 µmol/L or < 25 mg/dL), hemolysis (Hb ≤ 0.621 mmol/L or < 1.0 g/dL), Ipmnia (Intrapalid < 17.1 mmol/L or 1500 mg/dL) and Biotin (< 123 mmol/L or 30 ng/mL).

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.

There is no high-dose hook effect at NT-proBNP concentrations up to 35400 pmol/L (300000 pg/mL).

In vitro tests were performed on 51 commonly used pharmaceuticals. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

In extremely rare cases (global incidence: < 1 in 10 million), patients may show discrepant results when tested with the assay kit (values < lower detection limit) due to a NT-proBNP genotypic variant.

For diagnostic purposes, the results should always be assessed in conjunction with the patient’s medical history, clinical examination and other findings.

Limits and ranges

Measuring range

5-35000 pg/mL or 0.6-4130 pmol/L (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 5 pg/mL (< 0.6 pmol/L). Values above the measuring range are reported as > 35000 pg/mL (> 4130 pmol/L) or up to 70000 pg/mL (8260 pmol/L) for 2-fold diluted samples.

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: 5 pg/mL (0.6 pmol/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, repeatability study, n = 21).

Dilution

Samples with NT-proBNP concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution is 1:2 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 1770 pmol/L or > 15000 pg/mL.

After manual dilution, multiply the result by the dilution factor.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

Dilutions of up to 1:10 may entail maximum deviations of 25 % from the theoretical value.

Clinical data

Interpretation of NT-proBNP values

With increasing age atherosclerosis and aging processes of the heart (e.g. fibrosis) result in cardiac dysfunction. Development of cardiac dysfunction is individually different and clinically asymptomatic in its early stages. NT-proBNP levels reflect cardiac function or dysfunction respectively. With increasing age elevated levels of NT-proBNP are more frequently found in apparently healthy individuals, thus reflecting the increasing frequency of cardiac dysfunction.

NT-proBNP values need to be interpreted in conjunction with the medical history, clinical findings and other information (e.g. imaging, laboratory findings, accompanying disorders, treatment effects).

Cutoff values

A number of studies support a decision threshold for NT-proBNP of 125 pg/mL. NT-proBNP values < 125 pg/mL exclude cardiac dysfunction with a high level of certainty in patients with symptoms suggestive of heart failure e.g. dyspnea. NT-proBNP values > 125 pg/mL may indicate cardiac dysfunction and are associated with an increased risk of cardiac complications (myocardial infarction, heart failure, death).

Recommended cutoffs in patients with diagnosed stable chronic heart failure

Patients with stable heart failure (n = 721) were compared to the reference group (n = 2264).

ROC plot analysis at the cutoff value of 125 pg/mL showed a sensitivity of 86 %, a specificity of 92 %, a negative predictive value (NPV), and a positive predictive value (PPV) of 96.7 % and 30.6 %, respectively.

Expected values NT-proBNP concentrations in the reference group are shown in the following tables. The most appropriate decision threshold apparent from these distributions is 125 pg/mL.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Reference group

The circulating NT-proBNP concentration was determined in samples from 1981 blood donors aged between 18 and 65 as well as 283 elderly patients aged between 59 and 90, both populations without known cardiac risks, symptoms or medical history.

The descriptive statistics for NT-proBNP concentrations (pg/mL) in the reference group are shown in the following table:

<table>
<thead>
<tr>
<th>All</th>
<th>Age (years)</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>95th percentile</th>
<th>97.5th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18-44</td>
<td>1323</td>
<td>35.6</td>
<td>30.2</td>
<td>20.4</td>
<td>97.3</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>45-55</td>
<td>408</td>
<td>49.3</td>
<td>63.3</td>
<td>30.7</td>
<td>121</td>
<td>172</td>
</tr>
<tr>
<td></td>
<td>55-64</td>
<td>398</td>
<td>72.6</td>
<td>84.4</td>
<td>47.3</td>
<td>198</td>
<td>263</td>
</tr>
<tr>
<td></td>
<td>65-74</td>
<td>102</td>
<td>107</td>
<td>85.9</td>
<td>85.1</td>
<td>285</td>
<td>349</td>
</tr>
<tr>
<td>2-75</td>
<td>33</td>
<td>211</td>
<td>152</td>
<td>174</td>
<td>526</td>
<td>738</td>
<td></td>
</tr>
</tbody>
</table>

2017-08, V 12.0 English
### Elecsys proBNP II

#### NYHA functional class

<table>
<thead>
<tr>
<th>Age Category</th>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>182</td>
<td>250</td>
<td>234</td>
<td>35</td>
</tr>
<tr>
<td>Mean</td>
<td>1016</td>
<td>1666</td>
<td>3029</td>
<td>3465</td>
</tr>
<tr>
<td>SD</td>
<td>1951</td>
<td>2035</td>
<td>4600</td>
<td>4453</td>
</tr>
<tr>
<td>Median</td>
<td>342</td>
<td>951</td>
<td>1571</td>
<td>1707</td>
</tr>
<tr>
<td>25th percentile</td>
<td>33.0</td>
<td>103</td>
<td>126</td>
<td>148</td>
</tr>
</tbody>
</table>

#### NYHA functional class

<table>
<thead>
<tr>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>95th percentile</td>
<td>3410</td>
<td>6567</td>
<td>10449</td>
</tr>
<tr>
<td>% &gt; 125 pg/mL</td>
<td>78.6</td>
<td>94.0</td>
<td>95.3</td>
</tr>
</tbody>
</table>

#### Patients presenting acute dyspnea - ICON (International Collaborative of NT-proBNP) study

NT-proBNP concentrations were determined in samples from 1256 patients presenting with acute shortness of breath to emergency departments at four hospitals. This population included patients with a prior history of hypertension, coronary artery disease, myocardial infarction, heart failure, or pulmonary disease. 720 subjects were found to be suffering from acute exacerbation of heart failure, while the remainder were determined to present dyspnea due to other causes. The descriptive statistics for NT-proBNP concentrations (pg/mL) for both groups are shown in the following table:

#### ICON Population

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>&lt; 50</th>
<th>50-75</th>
<th>&gt; 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>163</td>
<td>500</td>
<td>1209</td>
</tr>
<tr>
<td>SD</td>
<td>484</td>
<td>1239</td>
<td>2703</td>
</tr>
<tr>
<td>Median</td>
<td>42</td>
<td>121</td>
<td>327</td>
</tr>
<tr>
<td>25th percentile</td>
<td>5</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>75th percentile</td>
<td>16</td>
<td>44</td>
<td>139</td>
</tr>
<tr>
<td>97.5th percentile</td>
<td>104</td>
<td>402</td>
<td>910</td>
</tr>
<tr>
<td>Min.</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Max.</td>
<td>4386</td>
<td>10467</td>
<td>15725</td>
</tr>
</tbody>
</table>

#### Rule in cut-point

<table>
<thead>
<tr>
<th>Category</th>
<th>Optimal cut-point pg/mL</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>450</td>
<td>97</td>
<td>93</td>
<td>79</td>
<td>99</td>
<td>94</td>
</tr>
<tr>
<td>(n = 184)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-75</td>
<td>900</td>
<td>90</td>
<td>82</td>
<td>83</td>
<td>88</td>
<td>85</td>
</tr>
<tr>
<td>years</td>
<td>(n = 537)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 75</td>
<td>1800</td>
<td>85</td>
<td>73</td>
<td>92</td>
<td>55</td>
<td>83</td>
</tr>
<tr>
<td>years</td>
<td>(n = 535)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Rule out cut-point

<table>
<thead>
<tr>
<th>Category</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>99</td>
<td>60</td>
<td>77</td>
<td>98</td>
<td>83</td>
</tr>
</tbody>
</table>

#### Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

#### Precision

Precision was determined using Elecsys reagents, pooled human sera and controls in a modified protocol (EPS-A) of the CLSI (Clinical and Laboratory...
Elecsys proBNP II

Standards Institute): 6 times daily for 10 days (n = 60): repeatability on MODULAR ANALYTICS E170 analyzer, n = 21. The following results were obtained:

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean (pg/mL)</th>
<th>SD (pmol/L)</th>
<th>CV (pmol/L %)</th>
<th>Mean (pmol/L)</th>
<th>SD (pg/mL)</th>
<th>CV (pg/mL %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human serum 1</td>
<td>44.0</td>
<td>5.19</td>
<td>1.84</td>
<td>0.22</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>Human serum 2</td>
<td>126</td>
<td>14.9</td>
<td>3.06</td>
<td>0.36</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Human serum 3</td>
<td>2410</td>
<td>284</td>
<td>31.7</td>
<td>3.74</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Human serum 4</td>
<td>33606</td>
<td>3966</td>
<td>922</td>
<td>10.9</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>PC CARDII1</td>
<td>82.0</td>
<td>9.68</td>
<td>2.11</td>
<td>0.25</td>
<td>2.58</td>
<td></td>
</tr>
<tr>
<td>PC CARDII2</td>
<td>2318</td>
<td>274</td>
<td>27.3</td>
<td>3.22</td>
<td>1.18</td>
<td></td>
</tr>
</tbody>
</table>

b) PC CARDII = PrecControl Cardiac II

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean (pg/mL)</th>
<th>SD (pmol/L)</th>
<th>CV (pmol/L %)</th>
<th>Mean (pmol/L)</th>
<th>SD (pg/mL)</th>
<th>CV (pg/mL %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human serum 1</td>
<td>44.0</td>
<td>5.19</td>
<td>2.02</td>
<td>0.24</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>Human serum 2</td>
<td>126</td>
<td>14.9</td>
<td>3.23</td>
<td>0.38</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>Human serum 3</td>
<td>2410</td>
<td>284</td>
<td>44.2</td>
<td>5.22</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Human serum 4</td>
<td>33606</td>
<td>3966</td>
<td>1288</td>
<td>152</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>PC CARDII1</td>
<td>82.0</td>
<td>9.68</td>
<td>2.27</td>
<td>0.27</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>PC CARDII2</td>
<td>2318</td>
<td>274</td>
<td>36.6</td>
<td>4.32</td>
<td>1.6</td>
<td></td>
</tr>
</tbody>
</table>

T = 0.946 r = 0.996

The sample concentrations were between approximately 5 and 3002 pg/mL (approximately 0.6 and 3543 pmol/L).

Analytical specificity

The Elecsys proBNP II assay does not show any significant cross reactions with the following substances, tested with NT-proBNP concentrations of approximately 230 pg/mL and 2300 pg/mL (max. tested concentration):

<table>
<thead>
<tr>
<th>Cross-reactant</th>
<th>Concentration tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenomedullin</td>
<td>1.0 ng/mL</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>0.6 ng/mL</td>
</tr>
<tr>
<td>Angiotensin I</td>
<td>0.6 ng/mL</td>
</tr>
<tr>
<td>Angiotensin II</td>
<td>0.6 ng/mL</td>
</tr>
<tr>
<td>Angiotensin III</td>
<td>1.0 ng/mL</td>
</tr>
<tr>
<td>ANP&lt;sub&gt;28&lt;/sub&gt;</td>
<td>3.1 µg/mL</td>
</tr>
<tr>
<td>Arg-vasopressin</td>
<td>1.0 ng/mL</td>
</tr>
<tr>
<td>BNP&lt;sub&gt;32&lt;/sub&gt;</td>
<td>3.5 µg/mL</td>
</tr>
<tr>
<td>CNP&lt;sub&gt;22&lt;/sub&gt;</td>
<td>2.2 µg/mL</td>
</tr>
<tr>
<td>Endothelin</td>
<td>20 pg/mL</td>
</tr>
<tr>
<td>NT-proANP&lt;sub&gt;1-39&lt;/sub&gt;</td>
<td>3.5 µg/mL</td>
</tr>
<tr>
<td>NT-proANP&lt;sub&gt;31-67&lt;/sub&gt;</td>
<td>1.0 µg/mL</td>
</tr>
<tr>
<td>NT-proANP&lt;sub&gt;73-99&lt;/sub&gt;</td>
<td>1.0 µg/mL</td>
</tr>
<tr>
<td>Renin</td>
<td>50 ng/mL</td>
</tr>
<tr>
<td>Urodiolatin</td>
<td>3.5 µg/mL</td>
</tr>
</tbody>
</table>

Functional sensitivity

50 pg/mL (5.9 pmol/L) The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of 20 %.

References


Elecsys proBNP II


45 International patent application WO 2005/124364 assigned to F. Hoffmann-La Roche AG and Roche Diagnostics GmbH. The use of cardiac hormones for diagnosing the risk of suffering from a cardiovascular complication as a consequence of cardiotoxic medication.


For further information, please refer to the appropriate operator’s manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols
Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.roche.com for definition of symbols used):

<table>
<thead>
<tr>
<th>CONTENT</th>
<th>System</th>
<th>REAGENT</th>
<th>CALIBRATOR</th>
<th>STIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contents of kit</td>
<td>Analyzers/Instruments on which reagents can be used</td>
<td>Reagent</td>
<td>Calibrator</td>
<td>Volume after reconstitution or mixing</td>
</tr>
</tbody>
</table>

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