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## Instructions for use

# 2-CAT RIA

<sup>125</sup>I – Radioimmunoassay for the quantitative determination of  
Adrenaline (Epinephrine) and Noradrenaline (Norepinephrine) in plasma and urine.

For *in-vitro* diagnostic use only.

**REF** IB88165



**IVD** 400 kBq

## **1. Introduction**

### **1.1 Intended use and principle of the test**

<sup>125</sup>I – Radioimmunoassay for the quantitative determination of Adrenaline (Epinephrine) and Noradrenaline (Norepinephrine) in plasma and urine. For *in-vitro* diagnostic use only.

Adrenaline (epinephrine) and noradrenaline (norepinephrine) are extracted by using a cis-diol- specific affinity gel, acylated and then converted enzymatically.

The assay procedure follows the basic principle of radioimmunoassay, involving competition between a radioactive and a non-radioactive antigen for a fixed number of antibody binding sites. The amount of <sup>125</sup>I-labelled antigen bound to the antibody is inversely proportional to the analyte concentration of the sample. When the system is in equilibrium, the antibody bound radioactivity is precipitated with a second antibody in the presence of polyethylene glycol. The precipitate is counted in a gamma counter. Quantification of unknown samples is achieved by comparing their activity with a reference curve prepared with known standards.

### **1.2 Clinical application**

In humans the catecholamines adrenaline (epinephrine), noradrenaline (norepinephrine) and dopamine are neurotransmitters of the sympathetic nervous system and are involved in many physiological processes. The sympathetic nervous system sets the body to a heightened state of alert, also called as the body's fight-or-flight response.

In the human body the catecholamines and their metabolites indicate the adaption of the body to acute and chronic stress.

Next to the metanephrine/normetanephrine the catecholamines are important for the diagnosis and the follow-up of tumors of the sympathoadrenal system like the pheochromocytoma. The quantitative determination of catecholamines in urine is preferred for the diagnosis of these tumors, whereas the determination of catecholamines in plasma is medically sensible for the localization of the tumor and for function testing. Values above the cut-off can provide an indication for neuroendocrine tumors.

However, in literature various diseases like hypertension, cardiovascular diseases, schizophrenia and manic depression are described with different levels of catecholamines.

Therapeutic consequences should never be based on laboratory results alone even if all test results are in agreement with the items as under point "Procedural cautions, guidelines and warnings". Any laboratory result is only a part of the total clinical picture of the patient.

Only in cases where the laboratory results are in an acceptable agreement with the overall clinical picture of the patient it can be used for therapeutic consequences.

The test result itself should never be the sole determinant for deriving any therapeutic consequences.

## **2. Procedural cautions, guidelines, warnings and limitations**

### **2.1 Precautions, guidelines and warnings**

- (1) This kit is intended for professional use only. Users should have a thorough understanding of this protocol for the successful use of this kit. Only the test instruction provided with the kit is valid and has to be used to run the assay. Reliable performance will only be attained by strict and careful adherence to the instructions provided.
- (2) This assay was validated for a certain type of sample as indicated in *Intended Use* (please refer to Chapter 1). Any off-label use of this kit is in the responsibility of the user and the manufacturer cannot be held liable.
- (3) The principles of Good Laboratory Practice (GLP) have to be followed.
- (4) In order to reduce exposure to potentially harmful substances, wear lab coats, disposable protective gloves and protective glasses where necessary.
- (5) All kit reagents – with exception of Precipitating Reagent - and specimens should be brought to room temperature and mixed gently but thoroughly before use. Avoid repeated freezing and thawing of reagents and specimens.
- (6) For the dilution or reconstitution purposes use deionized, distilled, or ultra-pure water.
- (7) The radioactive material (<sup>125</sup>Iodine, half life 60 days, emitting ionizing X-radiation with 28 keV and G-radiation with 35.5 keV) may be received, acquired, possessed and used only by physicians, laboratories or hospitals. In compliance with regulations, a copy of the customer's current radioisotope license must be on file with the supplier. Orders cannot be shipped until the license is received by the supplier (Radiation Protection Act of June 30, 1989).
- (8) Duplicate determination of sample is highly recommended to be able to identify potential pipetting errors.
- (9) Once the test has been started, all steps should be completed without interruption. Make sure that the required reagents, materials and devices are prepared ready at the appropriate time.
- (10) Incubation times do influence the results. All tubes should be handled in the same order and time intervals.

- (11) To avoid cross-contamination of reagents, use new disposable pipette tips for dispensing each reagent, sample, standard and control.
- (12) A standard curve must be established for each run.
- (13) The controls should be included in each run and fall within established confidence limits. The confidence limits are listed in the QC-Report provided with the kit.
- (14) Do not mix kit components with different lot numbers within a test and do not use reagents beyond expiry date as shown on the kit labels.
- (15) For information on hazardous substances included in the kit please refer to Material Safety Data Sheet (MSDS). The Material Safety Data Sheet for this product is available directly on the website or upon request.
- (16) The expected reference values reported in this test instruction are only indicative. It is recommended that each laboratory establishes its own reference intervals.
- (17) The results obtained with this test kit should not be taken as the sole reason for any therapeutic consequence but have to be correlated to other diagnostic tests and clinical observations.
- (18) Kit reagents must be regarded as hazardous waste and disposed of according to national regulations.

## 2.2 Limitations

Any inappropriate handling of samples or modification of this test might influence the results.

### 2.2.1 Interfering substances

#### Plasma

Samples containing precipitates or fibrin strands or which are haemolytic or lipemic might cause inaccurate results.

#### 24-hour urine

Please note the sample preparation! If the percentage of the final concentration of acid is too high, the buffer capacity of the Extraction Buffer is insufficient. As a consequence catecholamines will not be extracted adequately.

### 2.2.2 Drug interferences

There are no known substances (drugs) which ingestion interferes with the measurement of catecholamine level in the sample.

### 2.2.3 High-Dose-Hook effect

No hook effect was observed in this test.

## 3. Storage and stability

Store the unopened reagents at 2 - 8 °C until expiration date. Do not use components beyond the expiry date indicated on the kit labels. Once opened the reagents are stable for 1 month when stored at 2 - 8 °C.

## 4. Materials

### 4.1 Contents of the kit

**BA D-0090**      **FOILS**                      **Adhesive Foil** - Ready to use

Contents:        Adhesive Foils in a resealable pouch

Volume:         1 x 4 foils

**BA R-0025**      **PREC-REAG**                      **Precipitating Reagent** - Ready to use

Contents:        Goat anti-rabbit serum in PEG phosphate buffer

Volume:         2 x 55 ml/vial, white cap

**BA R-6618**      **EXTRACT-PLATE 48**              **Extraction Plate** - Ready to use

Contents:        2 x 48 well plates coated with boronate affinity gel in a resealable pouch


**BA R-0050**      **ADJUST-BUFF**                      **Adjustment Buffer** - Ready to use

Contents:        TRIS buffer

Volume:         1 x 4 ml/vial, green cap

**BA R-0120** <sup>125</sup>I ADR MN **<sup>125</sup>I – Adrenaline** - Ready to useContents: <sup>125</sup>I labeled Adrenaline, red coloured


Volume: 1 x 5.5 ml/vial, blue cap

Hazards identification: 

Radioactive, activity &lt; 200 kBq

**BA R-0220** <sup>125</sup>I NAD NMN **<sup>125</sup>I – Noradrenaline** - Ready to useContents: <sup>125</sup>I labeled Noradrenaline, red coloured

Volume: 1 x 5.5 ml/vial, yellow cap

Hazards identification: 

Radioactive, activity &lt; 200 kBq

**BA R-6110** AS ADR MN **Adrenaline Antiserum** - Ready to use

Contents: Rabbit anti- Adrenaline antibody, blue coloured

Volume: 1 x 5.25 ml/vial, blue cap

**BA R-6210** AS NAD **Noradrenaline Antiserum** - Ready to use

Contents: Rabbit anti- Noradrenaline antibody, yellow coloured

Volume: 1 x 5.25 ml/vial, yellow cap

**Standards and Controls** - Ready to use

Cat. no.	Component	Colour/ Cap	Concentration ng/ml		Concentration nmol/l		Volume/ Vial
			ADR	NAD	ADR	NAD	
<b>BA R-6601</b>	STANDARD A	white	0	0	0	0	4 ml
<b>BA R-6602</b>	STANDARD B	light yellow	1	5	5.5	30	4 ml
<b>BA R-6603</b>	STANDARD C	orange	4	20	22	118	4 ml
<b>BA R-6604</b>	STANDARD D	dark blue	15	75	82	443	4 ml
<b>BA R-6605</b>	STANDARD E	light grey	50	250	273	1 478	4 ml
<b>BA R-6606</b>	STANDARD F	black	200	1 000	1 092	5 910	4 ml
<b>BA R-6651</b>	CONTROL 1	light green	Refer to QC-Report for expected value and acceptable range!				4 ml
<b>BA R-6652</b>	CONTROL 2	dark red					4 ml

Conversion: Adrenaline (ng/ml) x 5.46 = Adrenaline (nmol/l)

Noradrenaline (ng/ml) x 5.91 = Noradrenaline (nmol/l)

Contents: Acidic buffer with non-mercury stabilizer, spiked with defined quantity of adrenaline and noradrenaline

**BA R-6611** ACYL-BUFF **Acylation Buffer** - Ready to use

Contents: Buffer with light alkaline pH

Volume: 1 x 20 ml/vial, white cap

**BA R-6613** ASSAY-BUFF **Assay Buffer** - Ready to use

Contents: 1M hydrochloric acid and a non-mercury preservative

Volume: 1 x 6 ml/vial, light grey cap

**BA R-6612** ACYL-REAG **Acylation Reagent** - Ready to use

Contents: Acylation reagent in DMF and DMSO

Volume: 1 x 3 ml/vial, light red cap

Hazards identification:   

H225 Highly flammable liquid and vapour.

H360 May damage fertility or the unborn child.

H319 Causes serious eye irritation.

<b>BA R-6614</b>	<b>COENZYME</b>	<b>Coenzyme</b> - Ready to use
Contents:	S-adenosyl-L-methionine	
Volume:	1 x 4 ml/vial, purple cap	
<b>BA R-6615</b>	<b>ENZYME</b>	<b>Enzyme</b> - Lyophilized
Contents:	Catechol-O-methyltransferase	
Volume:	4 vials, pink cap	
<b>BA R-6617</b>	<b>EXTRACT-BUFF</b>	<b>Extraction Buffer</b> - Ready to use
Contents:	Buffer containing carbonate	
Volume:	1 x 6 ml/vial, brown cap	
<b>BA R-6619</b>	<b>HCL</b>	<b>Hydrochloric Acid</b> - Ready to use
Contents:	0.025 M Hydrochloric Acid, yellow coloured	
Volume:	1 x 20 ml/vial, dark green cap	

#### 4.2 Additional materials and equipment required but not provided in the kit

- Calibrated precision pipettes to dispense volumes between 10 - 1000 µl
- Polystyrene tubes and suitable rack
- Temperature controlled water bath, heating block or incubator (37 °C)
- Centrifuge capable of at least 3,000 x g
- Suitable device for aspirating or decanting
- Shaker (shaking amplitude 3 mm; approx. 600 rpm)
- Gamma counter
- Vortex mixer
- Absorbent material (paper towel)
- Water (deionized, distilled or ultra-pure)

#### 5. Sample collection and storage

##### **Plasma**

Whole blood should be collected by venipuncture into centrifuge tubes containing EDTA as anti-coagulant (e.g. Monovette™ or Vacuette™ for plasma) and centrifuged at room temperature immediately after collection.

Haemolytic and especially lipemic samples should not be used for the assay.

Storage: up to 6 hours at 2 - 8 °C, for longer period (up to 6 month) at -20 °C.

Repeated freezing and thawing should be avoided.

##### **Urine**

Spontaneous urine or 24-hour urine, collected in a bottle containing 10 - 15 ml of 6 M HCl, can be used.


*If 24-hour urine is used please record the total volume of the collected urine.* If the percentage of the final concentration of acid is too high, the buffer capacity of the Extraction Buffer is insufficient. As a consequence catecholamines will not be extracted adequately.

Storage: up to 48 hours at 2 - 8 °C, up to 24 hours at room temperature, for longer periods (up to 6 month) at -20 °C. Repeated freezing and thawing should be avoided.

Avoid exposure to direct sunlight.

#### 6. Test procedure


Allow all reagents – with the exception of Precipitating Reagent - to reach room temperature and mix thoroughly by gentle inversion before use. Number the assay tubes accordingly. Duplicates are recommended.

 *Pipetted liquids should not adhere to the wall of the RIA tubes. If necessary please centrifuge the tubes for 1 minute at 500 x g to spin down adhering liquids.*


##### 6.1 Preparation of reagents

###### **Enzyme Solution**

Reconstitute the content of the vial labelled 'Enzyme' with 1 ml water (deionized, distilled or ultra-pure) and mix thoroughly. Add 0.3 ml of Coenzyme followed by 0.7 ml of Adjustment Buffer. The total volume of the Enzyme Solution is 2.0 ml.

 *The Enzyme Solution has to be prepared freshly prior to the assay (not longer than 10 - 15 minutes in advance). Discard after use!*

## 6.2 Sample preparation, extraction and acylation

1.	Pipette <b>10 µl</b> of <b>standards</b> and <b>controls</b> , <b>10 µl</b> of <b>urine samples</b> and <b>300 µl</b> of <b>plasma samples</b> into the respective wells of the <b>Extraction Plate</b> .		
2.	Add <b>250 µl</b> of <b>water</b> (deionized, distilled, or ultra-pure) to the wells with <b>standards, controls</b> and <b>urine samples</b> .		
3.	Pipette <b>50 µl</b> of <b>Assay Buffer</b> into all wells.		
4.	Pipette <b>50 µl</b> of <b>Extraction Buffer</b> into all wells.		
5.	Cover the plate with adhesive foil. Incubate for <b>30 min</b> at <b>RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm).		
6.	Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material.		
7.	Pipette <b>1 ml water</b> (deionized, distilled or ultra-pure) into all wells. Incubate the plate for <b>5 min</b> at <b>RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm). Empty plate and blot dry by tapping the inverted plate on absorbent material.		
8.	Pipette <b>150 µl</b> of <b>Acylation Buffer</b> into all wells.		
9.	Pipette <b>25 µl</b> of <b>Acylation Reagent</b> into all wells.		
10.	Incubate <b>15 min</b> at <b>RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm).		
11.	Empty the plate. Blot dry by tapping the inverted plate on absorbent material.		
12.	Pipette <b>1 ml water</b> (deionized, distilled, or ultra-pure) into all wells. Incubate the plate for <b>5 min</b> at <b>RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm). Empty plate and blot dry by tapping the inverted plate on absorbent material.		
13.	Pipette <b>150 µl</b> of <b>Hydrochloric Acid</b> into all wells.		
14.	Cover plate with adhesive foil. Incubate <b>10 min</b> at <b>RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm). Remove the foil. <b>Do not decant the supernatant thereafter!</b>		
	The following volumes of the supernatant are needed for the subsequent RIA:		
<b>Adrenaline</b>	<b>100 µl</b>	<b>Noradrenaline</b>	<b>20 µl</b>

## 6.3 Adrenaline RIA

1.	Pipette <b>100 µl</b> of <b>Hydrochloric Acid</b> into the tubes for the <b>NSB</b> .
2.	Pipette <b>100 µl</b> of the <b>extracted standards, controls</b> and <b>samples</b> into the respective tubes.
3.	Pipette <b>25 µl</b> of <b>Enzyme Solution</b> (refer to 6.1) into all tubes ( <b>except totals</b> ).
4.	Mix thoroughly and incubate for <b>30 min</b> at <b>37 °C</b> .
5.	Pipette <b>50 µl</b> of the <b><sup>125</sup>I Adrenaline</b> into <b>all tubes</b> .
6.	Pipette <b>50 µl</b> of <b>Adrenaline Antiserum</b> into <b>all tubes (except totals and NSB)</b> ; mix thoroughly.
7.	Cover tubes. Incubate for <b>15 - 20 h</b> (overnight) at <b>2 - 8 °C</b> . <b>Alternatively incubate for 2 h at RT</b> (20 - 25 °C) on a <b>shaker</b> (approx. 600 rpm).
8.	Mix the chilled (2 - 8 °C) <b>Precipitating Reagent</b> thoroughly, pipette each <b>500 µl</b> into <b>all tubes (except totals)</b> , and mix on a vortex.
9.	Incubate for <b>15 min</b> at <b>2 - 8 °C</b> .
10.	Centrifuge for <b>15 min</b> at <b>3,000 x g</b> , if possible in a refrigerated centrifuge.
11.	<b>Decant</b> or aspirate the <b>supernatant</b> carefully ( <b>except totals</b> ). Blot the tubes dry and leave them upside for 2 minutes.
12.	<b>Count</b> all tubes for <b>1 min</b> in a gamma counter.

## 6.4 Noradrenaline RIA

1. Pipette <b>20 µl</b> of <b>Hydrochloric Acid</b> into the tubes for the <b>NSB</b> .
2. Pipette <b>20 µl</b> of the <b>extracted standards, controls</b> and <b>samples</b> into the respective tubes.
3. Pipette <b>25 µl</b> of <b>Enzyme Solution</b> (refer to 6.1) into all tubes ( <b>except totals</b> ).
4. Mix thoroughly and incubate for <b>30 min</b> at <b>37 °C</b> .
5. Pipette <b>50 µl</b> of the <b><sup>125</sup>I Noradrenaline</b> into <b>all tubes</b> .
6. Pipette <b>50 µl</b> of <b>Noradrenaline Antiserum</b> into <b>all tubes (except totals and NSB)</b> ; mix thoroughly.
7. Cover tubes. Incubate for <b>15 - 20 h</b> (overnight) at <b>2 - 8 °C</b> . <b>Alternatively incubate for 2 h at RT (20 - 25 °C) on a shaker (approx. 600 rpm).</b>
8. Mix the chilled (2 - 8 °C) <b>Precipitating Reagent</b> thoroughly, pipette each <b>500 µl</b> into <b>all tubes (except totals)</b> , and mix on a vortex.
9. Incubate for <b>15 min</b> at <b>2 - 8 °C</b> .
10. Centrifuge for <b>15 min</b> at <b>3,000 x g</b> , if possible in a refrigerated centrifuge.
11. <b>Decant</b> or aspirate the <b>supernatant</b> carefully ( <b>except totals</b> ). Blot the tubes dry and leave them upside for 2 minutes.
12. <b>Count</b> all tubes for <b>1 min</b> in a gamma counter.


## 7. Calculation of results

Measuring range		Adrenaline	Noradrenaline
	Urine	0.39 - 200 ng/ml	1.1 - 1,000 ng/ml
	Plasma	19 - 6,667 pg/ml	42 - 33,333 pg/ml

Subtract the mean cpm of the non-specific binding NSB from the mean cpm of standards, controls and samples.

The standard curve from which the concentrations in the samples can be read off, is obtained by plotting the percentage of (B-NSB)/ (B<sub>0</sub>-NSB) measured for the standards (linear, y-axis) against the corresponding standard concentrations (logarithmic, x-axis).

Use a non-linear regression for curve fitting (e.g. spline, 4- parameter, akima).

 *This assay is a competitive assay. This means: the counts are decreasing with increasing concentrations of the analyte. Counts found below the standard curve correspond to high concentrations of the analytes in the sample and are to be reported as being positive.*

### Urine samples and controls

The concentrations of the **urine samples** and the **Controls 1 & 2** can be read directly from the standard curve.

Calculate the 24 h excretion for each urine sample: **µg/24h = µg/l x l/24h**

### Plasma samples

The read concentrations of the **plasma samples** have to be **divided by 30**.

### Conversion

Adrenaline (ng/ml) x 5.46 = Adrenaline (nmol/l)

Noradrenaline (ng/ml) x 5.91 = Noradrenaline (nmol/l)

### Expected reference values

It is strongly recommended that each laboratory should determine its own reference values.

	Adrenaline	Noradrenaline
Urine	< 20 µg/day (110 nmol/day)	< 90 µg/day (535 nmol/day)
Plasma	< 100 pg/ml	< 600 pg/ml

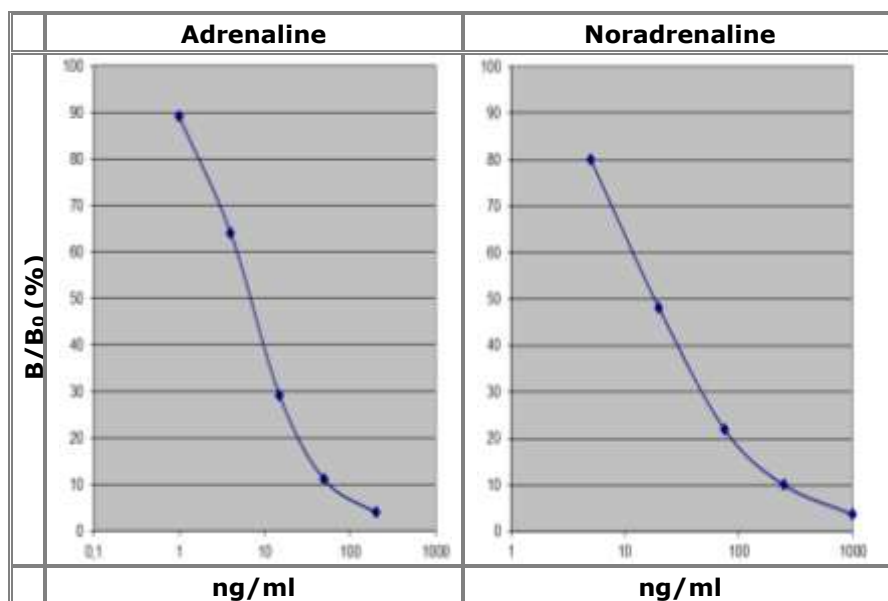
## 7.1 Quality control

It is recommended to use control samples according to national regulations. Use controls at both normal and pathological levels. The kit controls or other commercial controls should fall within established confidence limits. The confidence limits of the kit controls are printed on the QC-Report.

## 7.2 Typical standard curves



Examples, do not use for calculation!



## 8. Assay characteristics

Analytical Sensitivity (Limit of Detection)	Adrenaline		Noradrenaline	
	Urine	0.39 ng/ml	1.1 ng/ml	
	Plasma	19 pg/ml	42 pg/ml	

Analytical Specificity (Cross Reactivity)	Substance	Cross Reactivity (%)	
		Adrenaline	Noradrenaline
	Derivatized Adrenaline	100	0.08
Derivatized Noradrenaline	0.13	100	
Derivatized Dopamine	< 0.01	0.03	
Metanephrine	0.18	< 0.01	
Normetanephrine	< 0.01	0.16	
3-Methoxytyramine	< 0.01	< 0.01	
3-Methoxy-4-hydroxyphenylglycol	< 0.01	< 0.01	
Tyramine	< 0.0007	< 0.01	
Phenylalanine, Caffeinic acid, L-Dopa, Homovanillic acid, Tyrosine, 3-Methoxy-4-hydroxymandelic acid	< 0.01	< 0.01	

Precision							
Intra-Assay Urine (n = 40)				Intra-Assay Plasma (n = 40)			
	Sample	Range (ng/ml)	CV (%)		Sample	Range (ng/ml)	CV (%)
Adrenaline	1	15.8 ± 1.1	7.0	Adrenaline	1	146 ± 17.4	12.0
	2	22.3 ± 1.7	7.4		2	389 ± 38.7	10.1
	3	45.2 ± 5.1	11.3		3	1 271 ± 88.4	7.0
Noradrenaline	1	86.8 ± 6.8	7.8	Noradrenaline	1	992 ± 85.8	9.3
	2	122 ± 10.9	8.9		2	1 811 ± 224	12.3
	3	244 ± 21.9	8.9		3	4 935 ± 663	13.4



Inter-Assay Urine (n = 18)				Inter-Assay Plasma (n = 20)			
	Sample	Range (ng/ml)	CV (%)		Sample	Range (ng/ml)	CV (%)
Adrenaline	1	15.5 ± 1.5	9.5	Adrenaline	1	129 ± 12.7	9.8
	2	21.0 ± 2.5	11.7		2	347 ± 31.9	9.2
	3	42.7 ± 5.0	11.7		3	1 139 ± 128	11.3
Noradrenaline	1	77.7 ± 8.5	10.9	Noradrenaline	1	754 ± 184	24.4
	2	104 ± 9.4	9.1		2	1 661 ± 176	10.9
	3	198 ± 22.7	11.5		3	4 049 ± 391	9.7

Linearity			Serial dilution up to	Range (%)	Mean (%)
	Adrenaline	Urine	1:128	99 - 114	105
		Plasma	1:128	107 - 113	110
	Noradrenaline	Urine	1:128	93 - 106	98
		Plasma	1:128	95 - 113	103

Recovery			Concentration range	Range (%)	Mean (%)
	Adrenaline	Urine	5.2 - 48.8 ng/ml	101 - 111	105
		Plasma	25.3 - 1 001 pg/ml	105 - 119	111
	Noradrenaline	Urine	62.9 - 292 ng/ml	99 - 107	102
		Plasma	377 - 4 457 pg/ml	80 - 101	92

Method Comparison versus HPLC*	Noradrenaline	Urine	HPLC = 1.23 RIA - 0.12	r = 0.99; n = 21
		Plasma	HPLC = 1.27 RIA - 0.14	r = 0.99; n = 20
	Adrenaline	Urine	HPLC = 0.95 RIA - 0.03	r = 0.99; n = 21
		Plasma	HPLC = 0.80 RIA - 0.03	r = 0.96; n = 20













\*The concentrations were assessed using both the RIA and the HPLC method (external QC samples from UK NEQAS). The correlation between RIA and HPLC is excellent. This means, that the RIA measure equally good when compared to the UK NEQAS HPLC data. Please take in mind, that the UK control values are the mean of about 40 different HPLC users, and contain always one pathological sample per sending.

## 9. References/Literature

- (1) Rostrum et al. Physiological effects of combined thermal and electrical muscle stimulation (cTEMS) in healthy individuals A pilot study. Scandinavian Journal of Clinical and Laboratory Investigation, 72(3):237-245 (2012)
- (2) Milman et al. Opioid Receptor Blockade Prevents Exercise-Associated Autonomic Failure in Humans. Diabetes, 61(6):1609-1615 (2012)
- (3) Vele et al. Opioid Receptor Blockade Improves Hypoglycemia-Associated Autonomic Failure in Type 1 Diabetes Mellitus. The Journal of Clinical Endocrinology & Metabolism, 96(11): 3424-3431 (2011)

 **For updated literature or any other information please contact your local supplier.**

### Symbols:

	Storage temperature		Manufacturer		Contains sufficient for <n> tests
	Expiry date		Batch code		For in-vitro diagnostic use only!
	Consult instructions for use		Content		CE labelled
	Caution		Catalogue number		For research use only!