BECKMAN COULTER

CE 2797

Cortisol Sensitive RIA

Instruction for use in local language is available at beckmancoulter.com/techdocs.

REVISION HISTORY

Previous version: IFU-C23117-C23118-01	**Current version:** IFU-C23117-C23118-02
APPENDIX —	Changed data in columns Expected and Measured concentration in the Recovery chapter.
Specificity table in the chapter APPENDIX. —	17α-hydroxypregnanolone, Pregnanetriol and Pregnanetriolone were added to the table.
Radioactivity table in the chapter APPENDIX. —	Better specification of Iodine 125 characteristics table at the end of the chapter Appendix.

REF C23117, C23118

FOR PROFESSIONAL USE ONLY

INTENDED PURPOSE

Cortisol Sensitive RIA is an in vitro diagnostic manual medical device intended to be used by healthcare professionals for the quantitative measurement of cortisol in human serum, plasma, urine or saliva. Measurement of cortisol is intended to be used as an aid in diagnosis of adrenal related disorders, such as Cushing's syndrome and Addison's Disease in general population [1, 2, 3, 4, 5, 6].

PRINCIPLE

The radioimmunoassay of cortisol is a competition assay. Samples and calibrators are incubated with ^{125}I-labeled cortisol, as a tracer, in monoclonal antibody-coated tubes. After incubation, the contents of the tubes are aspirated so as to remove unbound ^{125}I-labeled tracer. The bound radioactivity is then determined in a gamma counter. The cortisol concentrations in the samples are obtained by interpolation from the standard curve. The concentration of cortisol in the samples is indirectly proportional to the radioactivity.

WARNING AND PRECAUTIONS

General remarks:

- The vials with calibrators and controls should be opened as shortly as possible to avoid excessive evaporation.
- Do not mix the reagents from kits of different lots.
- A standard curve must be established with each assay.
- It is recommended to perform the assay in duplicate.
- Each tube must be used only once.

Protection against ionizing radiation

The purchase, possession, utilization, and transfer of radioactive material is subject to the regulations of the country of use. Adherence to the basic rules of radiation safety should provide adequate protection.

- No eating, drinking, smoking or application of cosmetics should be carried out in the presence of radioactive materials.
- No pipetting of radioactive solutions by mouth.
- Avoid all contact with radioactive materials by using gloves and laboratory overalls.
- All manipulation of radioactive substances should be done in an appropriate place, distant from corridors and other busy places.
- Radioactive materials should be stored in the container provided in a designated area.
- A record of receipt and storage of all radioactive products should be kept up to date.
- Laboratory equipment and glassware which are subject to contamination should be segregated to prevent cross-contamination of different radioisotopes.
- Each case of radioactive contamination or loss of radioactive material should be resolved according to established procedures.
- Radioactive waste should be handled according to the rules established in the country of use.

Sodium azide

Some reagents contain sodium azide as a preservative. Sodium azide can react with lead, copper or brass to form explosive metal azides. Sodium azide disposal must be in accordance with appropriate local regulations.

Material of human origin

All patient specimens should be handled as potentially infectious and waste should be discarded according to the country rules.

Dichloromethane

Dichloromethane is a highly volatile and inflammable solvent. Extraction and evaporation must be done in a ventilated hood. Keep away from any open flame. Do not pipet reagents by mouth.

The summary of safety and performance for this in vitro diagnostic medical device is available to the public in the European database on medical device (EUDAMED) when this database is available, and the information has been uploaded by the Notified Body. The web address of the EUDAMED public web site is: https://ec.europa.eu/tools/eudamed.

GHS HAZARD CLASSIFICATION

Not classified as hazardous

SDS Safety Data Sheet is available at beckmancoulter.com/techdocs

SPECIMEN COLLECTION, PROCESSING, STORAGE AND DILUTION

Serum and plasma samples

- Serum or EDTA plasma are the recommended sample types.
- Allow serum samples to clot completely before centrifugation.
- Serum and plasma samples may be stored at 2-8°C, if the assay is to be performed within 24 hours. For longer storage keep frozen (at < -18°C, 1 year maximum), after aliquoting so as to avoid repeated freezing and thawing. Thawing of sample should be performed at room temperature.
- If samples have concentrations greater than the highest calibrator, they must be diluted into the zero calibrator.

Urine samples

- Collect 24-hour urine in flask.
- Determine volume.
- If necessary, store aliquoted at < -18°C, 1 year maximum. Thawing of sample should be performed at room temperature.
- If samples have concentrations greater than the highest calibrator, they must be diluted in distilled water.

Saliva samples

- Collect saliva using swab, which is placed in the mouth and chewed for 60 seconds to stimulate salivation.
- Separate saliva from swab into conical tube by centrifugation for 2 minutes at 1,000xg.
- Store at 2-8°C for up to 3 months. For longer storage keep frozen at < -18°C, up to 1 year.

MATERIALS PROVIDED

All reagents of the kit are stable until the expiry date indicated on the kit label, if stored at 2-8°C. Expiry dates printed on vial labels apply to the long-term storage of components by the manufacturer only, prior to assembly of the kit. Do not take into account.

Kit for determination of cortisol, 100 tubes (REF. C23117)

Tubes: 2 x 50 (ready-to-use)

^{125}I-Tracer: one 55 mL vial (ready-to-use)

The vial contains 185 kBq, at the date of manufacture, of ^{125}I-labeled cortisol in buffer containing bovine serum albumin, sodium azide (<0.1%) and a dye.

Calibrators: five 0.5 mL vials and one 5 mL vial of «zero» calibrator (ready-to-use)

The calibrator vials contain from 0 to approximately 2,000 nM of cortisol in buffer with bovine serum albumin and sodium azide (<0.1%). The exact concentration is indicated on each vial label. The calibrators are traceable to reference preparations ERM-DA192 and 193.

The zero calibrator may be ordered separately, too (REF. IM1959 - 10 mL, REF. IM3444 - 250 mL).

Note: Occasional presence of turbidity in the zero calibrator does not affect assay performance.

Control sample: one 0.5 mL vial (ready-to-use)

The vial contains cortisol in a buffer with bovine serum albumin and sodium azide (<0.1%). The concentration range is indicated on a supplement. The control sample is traceable to reference preparations ERM-DA192 and 193.

Kit for determination of cortisol, 50 tubes (REF. C23118)

Tubes: 1 x 50 (ready-to-use)

^{125}I-Tracer: one 55 mL vial (ready-to-use)

Calibrators: five 0.5 mL vials and one 5 mL vial of «zero» calibrator (ready-to-use)

Control sample: one 0.5 mL vial (ready-to-use)

MATERIALS REQUIRED, BUT NOT PROVIDED

In addition to standard laboratory equipment, the following items are required:

- Precision micropipette (50 µL).
- Semi-automatic pipette (500 µL).
- Vortex type mixer.
- Horizontal or orbital shaker.
- Aspiration system.
- Gamma counter set for ^{125}I.

For the assay of urine extract cortisol (optional)

- Precision micropipette (200 µL).
- Analytical grade dichloromethane (methylene chloride), not ethanol-stabilized.
- Glass tubes or vials fitted with teflon-lined screw caps.
- 2 and 5 mL glass pipets.
- Evaporator.

For the assay of saliva

- Salivette REF. C19926; 100 pcs.
- Buffer for calibrator and control dilution (PBS pH 7.2, may be also ordered under REF. C19927; 15 mL)
- Precision micropipette (300 µL).
- Centrifuge.

PROCEDURE

Extraction of urine (optional, see Assay procedure for direct assay of urine cortisol).

Note: The extraction must be done in clean glass vials or tubes, pre-rinsed with dichloromethane and fitted with teflon or glass stoppers.

Bring samples to room temperature and mix well before starting extraction.

Samples only are extracted before assay; do not extract calibrators.

- Cool a sufficient volume of dichloromethane in ice-water bath.
- Number tubes or flasks.
- Add 500 µL of urine sample to numbered tubes kept on ice.
- Add 5 mL of dichloromethane using a glass pipet, stopper carefully and vortex for one minute.
- Let the two phases separate at room temperature.
- Take off upper, aqueous phase by aspiration.
- Take 2 mL of organic phase using glass pipet or syringe.
- Evaporate organic phase completely in evaporator. Do not heat.
- Re-dissolve organic extract in 200 µL of zero calibrator. Wait 15 minutes and then vortex vigorously.

Preparation of reagents

Let all the reagents come to room temperature.

Assay procedure for serum, plasma and urine extracts:

Step 1 Additions*	Step 2 Incubation	Step 3 Counting
To coated tubes, add successively: 50 µL of calibrator, control, serum sample, plasma sample or urine extract and 500 µL of tracer. Vortex gently 1-2 seconds.	Incubate 1 hour at 18-25°C with shaking (≥ 400 rpm).	Aspirate carefully the content of tubes (except the 2 tubes «total cpm»). Count bound cpm (B) and total cpm (T) for 1 min.

*. Add 500 µL of tracer to 2 additional tubes to obtain total cpm.

Assay procedure for direct assay of urine cortisol:

Step 1 Additions*	Step 2 Incubation	Step 3 Counting
To coated tubes, add successively: 50 µL of calibrator or control or 50 µL of urine sample followed by 50 µL of zero calibrator** and 500 µL of tracer. Vortex gently 1-2 seconds.	Incubate 1 hour at 18-25°C with shaking (≥ 400 rpm).	Aspirate carefully the content of tubes (except the 2 tubes «total cpm»). Count bound cpm (B) and total cpm (T) for 1 min.

*. Add 500 µL of tracer to 2 additional tubes to obtain total cpm.

**. Additional 50 µL of zero calibrator is added to tubes with urine samples only.

Assay procedure for saliva:

Dilute ten times calibrators and control samples with buffer for dilution - PBS (0.15 M phosphate buffer, pH 7.2), e.g. add 70 µL of calibrator or control in 630 µL of PBS and mix. Do not dilute saliva samples. Buffer for dilution is available separately, too (REF. C19927).

Step 1 Additions	Step 2 Incubation	Step 3 Counting
To coated tubes, add successively: 300 µL of calibrator, control or saliva sample and 500 µL of tracer. Vortex gently 1-2 seconds.	Incubate 1 hour at 18-25°C with shaking (≥ 400 rpm).	Aspirate carefully the content of tubes (except the 2 tubes «total cpm»). Count bound cpm (B) and total cpm (T) for 1 min.

· * Add 100 µL of tracer to 2 additional tubes to obtain total cpm.

RESULTS

Results are obtained from the calibrator curve by interpolation. The curve serves for the determination of analyte concentrations in samples measured at the same time as the calibrators.

Standard curve

The results in the quality control department were calculated using *spline* curve fit with logit of *B/T or B/B_0* on the vertical axis and log of analyte concentration of the calibrators on the horizontal axis.

Other calculation methods may give slightly different results.

Serum, plasma and urine:

Total activity: 55,916 cpm				
Calibrators	**Cortisol (nM)**	**cpm (n=2)**	**B/T (%)**	**B/B_0 (%)**
0	0	47,997	85.4	100.0
1	9.8	43,019	76.9	89.6
2	50	30,051	53.7	62.6
3	200	14,480	25.9	30.2
4	720	5,682	10.2	11.8
5	2,400	2,398	4.29	5.00

· *(Example of standard curve, do not use for calculation).*

Saliva:

Total activity: 55,003 cpm				
Calibrators	**Cortisol (nM)**	**cpm (n=2)**	**B/T (%)**	**B/B_0 (%)**
0	0	45,424	82.6	100.0
1	0.98	42,742	77.7	94.1
2	5.0	36,287	66.0	79.9
3	20	23,075	42.0	50.8
4	72	9,942	18.1	21.9
5	240	4,038	7.34	8.89

· *(Example of standard curve, do not use for calculation).*

Samples

For each sample, locate ratio B/T or B/B_0 on the vertical axis and read off the corresponding analyte concentration on the horizontal axis.

To convert concentrations from nmol/L to ng/mL, multiply results by 0.362.

Serum, plasma or urine samples assayed after extraction

The concentration is in nanomoles per liter (nM). The calculation of the daily urinary cortisol excretion is given in the following paragraph.

Urine samples assayed by direct procedure

The value must be multiplied by **1.09**, the dilution factor due to the addition of 50 µL of zero calibrator.

It is suggested that in cases where there is disagreement with clinical data or other measurements, to check the value obtained in the direct assay by an indirect assay after dichloromethane extraction.

The daily excretion of urine cortisol (Q) (nmol/24hours) is:

$$Q = U \times V$$

where

U = urine cortisol value (nM)

V = volume of urine in liters/24 hours

Saliva samples

Cortisol concentrations are obtained from salivary calibration curve, with values 10x lower than those of original kit calibrators to reflect their dilution.

EXPECTED VALUES

We recommend each laboratory to establish its own reference values. The following values obtained from healthy subjects are indicative only.

Serum:

Morning: 263 to 724 nM (n = 69) Evening: 49 to 430 nM (n = 84)

Detail information about expected values for children (sorted according to age and sex) can be found in the data sheet "APPENDIX".

Urines (n = 66)

Assay	Mean (nmol/24h)	Standard deviation (nmol/24h)	Extreme values for 95% of population (nmol/24h)
Direct	114	55	38 - 208
After extraction	103	45	30 - 197

Saliva:

Adults	**N**	**Median**	**Min.**	**Max.**	**2.5th percentile**	**97.5th percentile**
				(nM)		
Morning values (just after waking up)	37	8.05	4.26	20.31	4.40	20.26
AM values (9-12)	31	2.42	< 0.8	9.27	1.02	7.99
PM values (14-18)	33	1.19	< 0.8	3.71	< 0.8	2.75
Night values (after 20)	35	< 0.8	< 0.8	2.77	< 0.8	2.57

QUALITY CONTROL

Good laboratory practices imply that control samples be used regularly to ensure the quality of the results obtained. These samples must be processed exactly in the same way as the assay samples, and it is recommended that their results be analyzed using appropriate statistical methods.

Failure to obtain the appropriate values for controls may indicate imprecise manipulations, improper sample handling or deterioration of reagents.

In case of packaging deterioration or if data obtained show some performance alteration, please contact your local distributor or use the following e-mail address: imunochem@beckman.com

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of EU Member State in which the user and/or patient is located.

PERFORMANCE CHARACTERISTICS

(For more details, see the data sheet "APPENDIX")

Representative data are provided for illustration only. Performance obtained in individual laboratories may vary.

Analytical sensitivity:

Serum, plasma, urine, urine extracts: 4.23 nM

Saliva protocol: 0.80 nM

Specificity

The antibody used in the immunoassay is highly specific for cortisol. Extremely low cross reactivities were obtained against other naturally occurring steroids (Aldosterone, Corticosterone, Cortisone, 11-Desoxycortisol, Progesterone, etc.) or therapeutic drugs that may be present in patient samples (Prednisolone, Prednisone, Spironolactone, etc.).

Precision

Intra-assay

Samples were assayed 25 times in the same series. The coefficients of variation were found below or equal to 12.6% for serum samples.

Inter-assay

Samples were assayed in duplicate in 10 different series. Coefficients of variation were found below or equal to 12.7% for serum samples.

Accuracy

Dilution test

High-concentration samples were serially diluted with the zero calibrator. The recovery percentages obtained were between 81.5% and 106.6% for serum samples.

Recovery test

Low-concentration samples were spiked with known quantities of cortisol. The recovery percentages obtained were between 100.5% and 115.1% for serum samples.

Measurement range (from analytical sensitivity to the highest calibrator): 4.23 to approximately 2,000 nM.

Measurement range (from analytical sensitivity to the highest calibrator): 0.8 to approximately 200 nM for saliva protocol.

LIMITATIONS

Failure to follow these instructions for use (IFU) may significantly affect results.

Results should be interpreted in the light of the total clinical presentation of the patient, including clinical history, data from additional tests and other appropriate information.

Sallivettes containing citric acid are not recommended for the collection of saliva.

Do not use hemolyzed, lipemic or icteric samples. For more details, see Appendix, § Interference.

In spite of the very low cross-reactivity with corticoids currently employed therapeutically, particularly prednisolone and prednisone, treatment with high doses may lead to an artefactual increase in serum and urine cortisol, due to interference by the substance administered or certain of its metabolites. It is therefore inadvisable to perform direct cortisol assays on patients receiving systemic corticotherapy.

In immunoassays, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Immunoassays may be also affected by presence of anti-avidin or anti-streptavidin antibodies, as well as by the presence of autoantibodies directed against the determined analyte. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies [7, 8, 9].

APPENDIX

PERFORMANCE CHARACTERISTICS

Representative data are provided for illustration only. Performance obtained in individual laboratories may vary.

Interference

Serum samples containing cortisol concentrations (low and high) were spiked with multiple concentrations of the substances listed below and assayed using Cortisol Sensitive RIA. Values were calculated as described in CLSI EP07, 3rd ed. [10]. Interference was determined by testing controls (no interfering substance added) and matched test samples (with interfering substance added). No interference (defined as a shift in dose > 15%) was found for addition of interferent up to concentration stated in the table below.

Interferent	Test concentration
Biotin	1,554 ng/mL
Conjugated bilirubin	493.3 µg/mL
Hemoglobin	10,443 µg/mL
Prednisone	125.1 ng/mL
Prednisolone	84.49 ng/mL
Triglycerides	23.28 mg/mL
Unconjugated bilirubin	382.6 µg/mL

In spite of hemoglobin, bilirubin (conjugated, unconjugated), triglycerides, prednisone and prednisolone interference data in the table, we advise to avoid using hemolyzed, lipemic or icteric samples or samples of those patients who are receiving systemic corticotherapy.

Specificity

The percent cross-reactivity is expressed as the ratio of the cortisol concentration to the concentration of the reacting compound at 50% binding of the zero calibrator.

Data on cross-reactivity with some endogenous and pharmaceutically employed steroids are presented in the following table:

Steroid	% Cross- reactivity	Steroid	% Cross- reactivity
Cortisol	100	Tetrahydro-11-desoxycortisol	<0.1
11-Desoxycortisol	18	Dexamethasone	<0.1
Corticosterone	8.4	Substance E	<0.1
21-Desoxycortisol	7.5	α-Cortolone	<0.1
Desoxycorticosterone	7.3	Hydrocortisone-21-sulfate	<0.1
17α-Hydroxyprogesterone	3.5	Etiocholanolone	<0.1
Dihydrocortisol	2.4	11β-Hydroxyetiocholanolone	<0.1
5α-Dihydrocortisone	2.3	Prégnenolone sulfate	<0.1
5β-Dihydrocortisone	<0.1	Estradiol	<0.1
Progesterone	1.8	Estriol	<0.1
Cortisone	1.5	Estrone	<0.1
Pregnenolone	1.1	DHEA-sulfate	<0.1
Allotetrahydrocortisone	0.8	Androstenedione	<0.1
21-Desoxycortisone	0.13	Spironolactone	<0.1
6α-Methylprednisolone	0.27	18-Hydroxycorticosterone	<0.1
6β-Hydroxycortisol	<0.1	Aldosterone	<0.1
β-Cortolone	<0.1	Danazol	<0.1
20α-Dihydrocortisol	<0.1	5α-Dihydrotestosterone	<0.1
Tetrahydrocortisone	<0.1	19-Norethisterone	<0.1
β-Cortol	<0.1	Testosterone	<0.1
Tetrahydrocortisol	<0.1	Cholesterol	<0.1
17-hydroxypregnanolone	ND	Pregnanetriol	ND
Pregnanetriolone	ND		

· ND = Non-detectable

Precision

Intra-assay

Samples	Serum (n=25)			EDTA plasma (n=25)		
	S1	S2	S3	P1	P2	P3
Mean (nM)	175.7	1,216	2,899	152.5	874.6	3,181
CV (%)	12.64	6.0	8.0	6.63	5.3	5.47

Samples	Urine (direct) (n=25)			Urine (extract) (n=25)		
	U1	U2	U3	UE1	UE2	UE3
Mean (nM)	44.93	891.2	1,429	15.92	1,010	1,793
CV (%)	9.05	7.48	6.50	11.73	4.78	4.35

Samples	Saliva (n=25)		
	SA1	SA2	SA3
Mean (nM)	1.94	71.74	177.6
CV (%)	14.48	6.38	4.43

Inter-assay

Samples were assayed in duplicate.

Samples	Serum (n=10)			EDTA plasma (n=10)		
	S1	S2	S3	P1	P2	P3
Mean (nM)	332.2	1,005	1,545	182.1	1,013	2,385
CV (%)	8.10	12.72	12.46	6.16	8.47	11.23

Samples	Urine (direct) (n=10)			Urine (extract) (n=10)		
	U1	U2	U3	UE1	UE2	UE3
Mean (nM)	31.08	624.1	1,856	18.73	611.7	1,979
CV (%)	11.18	5.06	7.65	11.08	5.53	6.41

Samples	Saliva (n=10)		
	SA1	SA2	SA3
Mean (nM)	4.47	25.42	98.92
CV (%)	9.50	4.98	5.14

Accuracy

Dilution test

Serum, plasma samples and urine extracts were diluted in the zero calibrator, urine samples in the water and assayed according to the procedure of the kit.

Serum	Dilution factor	Measured	Expected	Ratio (%) Measured/ Expected
		(nM)		
S1	-	447.8	-	-
	1:2	238.7	223.9	106.6
	1:4	94.66	111.9	84.55
	1:8	45.85	55.98	81.91
	1:16	24.17	27.99	86.36
	1:32	11.40	13.99	81.46
S2	-	873.1	-	-
	1:2	433.6	436.5	99.32
	1:4	195.5	218.3	89.58
	1:8	92.23	109.1	84.51
	1:16	46.15	54.57	84.60
	1:32	26.67	27.28	97.80
S3	-	2,096	-	-
	1:2	997.8	1,048	95.21
	1:4	455.0	524.0	86.84
	1:8	232.5	262.0	88.75
	1:16	133.1	131.0	101.6
	1:32	62.42	65.50	95.30

EDTA plasma	Dilution factor	Measured	Expected	Ratio (%) Measured/ Expected
		(nM)		
P1	-	1,765	-	-
	1:2	861.5	882.5	97.62
	1:4	410.8	441.2	93.10
	1:8	193.0	220.6	87.46
	1:16	97.74	110.3	88.60
	1:32	51.79	55.15	93.89
P2	-	1,183	-	-
	1:2	565.0	591.7	95.48
	1:4	287.3	295.9	97.11
	1:8	138.5	147.9	93.63
	1:16	67.33	73.96	91.00
	1:32	38.97	36.98	105.4
P3	-	662.0	-	-
	1:2	319.7	331.0	96.58
	1:4	163.8	165.5	98.98
	1:8	72.80	82.75	87.97
	1:16	40.86	41.38	98.74
	1:32	23.47	20.69	113.4

Urine (direct)	Dilution factor	Measured	Expected	Ratio (%) Measured/ Expected
		(nM)		
U1	-	1,488	-	-
	1:2	639.5	744.2	85.93
	1:4	327.6	372.1	88.05
	1:8	149.6	186.0	80.39
U2	-	668.7	-	-
	1:2	335.3	334.3	100.3
	1:4	142.3	167.2	85.13
	1:8	69.45	83.59	83.09
U3	-	329.8	-	-
	1:2	170.4	164.9	103.3
	1:4	72.55	82.46	87.98
	1:8	33.18	41.23	80.48

Urine (extract)	Dilution factor	Measured	Expected	Ratio (%) Measured/ Expected
		(nM)		
UE1	-	1,152	-	-
	1:2	464.3	576.2	80.58
	1:4	238.0	288.1	82.60
	1:8	126.7	144.1	87.93
	1:16	57.83	72.03	80.29
UE2	-	553.8	-	-
	1:2	252.9	276.9	91.33
	1:4	125.0	138.5	90.29
	1:8	58.37	69.22	84.32
	1:16	29.93	34.61	86.50
UE3	-	1,055	-	-
	1:2	483.2	527.5	91.61
	1:4	240.4	263.7	91.15
	1:8	110.7	131.9	83.97
	1:16	58.37	65.93	88.53

Recovery test

Samples were spiked with known quantities of cortisol and assayed according to the assay procedure of the kit.

Serum	Endogen. conc.	Added conc.	Expected conc.	Measured conc.	Ratio (%) Measured/ Expected
	(nM)				
S1	23.43	13.29	36.71	37.37	101.8
	23.65	26.27	49.92	50.90	102.0
	22.99	44.68	67.67	68.00	100.5
S2	220.4	144.6	365.0	408.8	112.0
	217.2	285.0	502.2	562.7	112.1
	214.1	421.3	635.4	731.3	115.1
S3	659.1	285.0	944.0	1,001	106.0
	631.5	682.6	1,314	1,431	108.9
	617.1	889.4	1,507	1,707	113.3

EDTA plasma	Endogen. conc.	Added conc.	Expected conc.	Measured conc.	Ratio (%) Measured/ Expected
	(nM)				
P1	20.78	13.95	34.72	37.03	106.6
	20.98	29.41	50.39	45.37	90.04
	20.49	44.68	65.17	64.26	98.61
P2	263.6	106.6	424.2	438.5	103.4
	259.7	316.6	576.3	619.2	107.4
	256.0	468.0	724.1	715.5	98.82
P3	611.8	367.6	979.3	1,097	112.0
	586.3	805.1	1,391	1,536	110.4
	575.6	988.1	1,564	1,579	101.0

Urine (direct)	Endogen. conc.	Added conc.	Expected conc.	Measured conc.	Ratio (%) Measured/ Expected
	(nM)				
U1	46.3	17.3	63.6	67.8	106.6
	44.4	47.5	91.9	94.7	103
	45.7	101	147	140	95.3
U2	295	110	404	393	97.3
	296	355	651	655	100.6
	288	655	943	1,022	108.4
U3	963	355	1,318	1,526	115.9
	905	999	1,904	2,036	107
	972	2,183	3,155	3,145	99.7

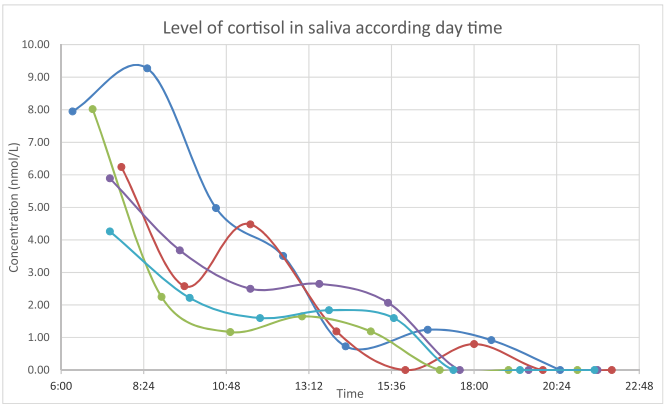
Urine (extract)	Endogen. conc.	Added conc.	Expected conc.	Measured conc.	Ratio (%) Measured/ Expected
	(nM)				
UE1	25.23	14.12	39.34	40.41	102.7
	25.48	23.76	49.24	52.69	107.0
	24.98	69.90	94.88	99.72	105.1
UE2	1,041	421.3	1,462	1,451	99.26
	1,002	946.3	1,948	1,833	94.10
	1,031	1,583	2,614	2,438	93.25
UE3	369.3	143.2	512.5	506.3	98.77
	365.7	283.6	649.3	663.4	102.2
	355.2	688.8	1044	993.9	95.19

Saliva	Endogen. conc.	Added conc.	Expected conc.	Measured conc.	Ratio (%) Measured/ Expected
	(nM)				
SA1	15.86	8.22	24.08	28.00	116.3
	16.17	16.09	33.26	35.71	110.7
	15.82	31.48	47.29	53.34	112.8
SA2	47.24	23.87	71.11	73.64	103.6
	48.04	40.45	88.49	91.04	102.9
	47.18	82.76	129.9	138.4	106.5
SA3	1.59	1.25	2.84	2.96	104.1
	1.56	2.05	3.62	3.58	98.95
	1.50	3.95	5.45	5.99	109.9

Expected serum values for children

Children	N	Median	Min	Max	2.5th percentile	97.5th percentile
		(nM)				
Girls						
< 1 month	16	89.5	35.8	450.3	35.9	414.1
1 - 2 months	16	123.0	26.3	605.8	27.4	579.2
3 - 5 months	27	196.6	42.1	621.1	52.0	614.9
6 - 11 months	31	254.8	105.6	766.2	116.6	658.4
1 - 8 years	31	324.1	140.0	645.2	154.6	537.1
9 - 14 years	34	252.1	112.5	632.0	115.1	610.1
Boys						
< 1 month	26	150.3	59.6	472.5	62.6	416.4
1 - 2 months	28	161.6	33.4	653.0	43.3	641.9
3 - 5 months	14	353.9	120.5	516.5	130.5	500.3
6 - 11 months	46	218.2	80.3	686.2	117.4	570.3
1 - 8 years	36	377.9	153.9	682.1	167.6	676.7
9 - 14 years	31	274.3	126.5	484.1	180.4	476.4

Example daily profiles of salivary cortisol



Correlations

Serum and EDTA plasma values for 15 samples (serum values ranging from 230.0 to 721.9 nM) were compared using the C23117 Cortisol Sensitive RIA. Results are as follows:

[EDTA-plasma] = 1.213 [serum] - 68.154, R = 0.9756

Direct assay of urinary cortisol and after extraction for 30 urine samples (values of direct urinary cortisol ranging from 35.8 to 783.7 nM) were compared using the C23117 Cortisol Sensitive RIA kit.

Results are as follows: [Direct] = 1.0097 [Extraction] + 19.211, R = 0.99

^{125}I Characteristics

$T_{1/2}$ (^{125}I) = 1443 h = 60.14 d

^{125}I	E (MeV)	%
γ	0.035	6.5
K_α X-ray	0.027	112.5
K_β X-ray	0.031	25.4

Symbols Key

REF	Product Reference / Référence du produit / Produktreferenz / Riferimento prodotto / Número de referencia del producto / Referência do produto / Produktreferens / Κωδικός αναφοράς προϊόντος / 产品参考 / Gaminio nuoroda / Termékszám / Dane referencyjne produktu / Reference k produktu / Referenčné označenie výrobku / 제품 참조 자료 / Ürün Referansı / Ссылка на продукт / Референца за производ / 產品參考
IVD	In Vitro Diagnostic / Diagnostic in vitro / In-vitro-Diagnostikum / Diagnostica in vitro / Para diagnóstico in vitro / Diagnóstico in vitro / InVitro-diagnostik / Για διάγνωση in vitro / 体外诊断 / In vitro diagnostika / In vitro diagnosztikai felhasználásra / Diagnostyka in vitro / Diagnostika in vitro / 체외 진단 / İn Vitro Diagnostik / Диагностика in vitro / За ин витро диагностика / 體外診斷
CONTENTS	Contents / Contenu / Inhalt / Contenuto / Contenido / Conteúdo / Περιεχόμενο / 组成 / Rinkinio sudėtis / Tartalom / Zawartość / Obsah / Obsah / 내용물 / İçindekiler / Содержание / Съдържание / 目錄
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Σ	Contains sufficient for <n> tests / Contenu suffisant pour "n" tests / Inhalt ausreichend für <n> Prüfungen / Contenuto sufficiente per "n" saggi / Contenido suficiente para <n> ensayos / Conteúdo suficiente para "n" ensaios / Räcker till "n" antal tester / Περιεχόμενο επαρκές για "v" εξετάσεις / 含量足够 <n> 次测试 / Turinio pakanka < n > tyrim / <n> teszthez elegendő mennyiséget tartalmaz / Zawartość wystarcza na <n> testów / Lze použít pro <n> testů / Obsah vystačí na < n > testov / <n> 테스트에 대해 충분한 양 포함 / <n> sayıda test için yeterlidir / Содержит достаточно для количества тестов: <n> / Съдържа достатъчно за <n> теста / 內容物足夠執行 <n> 次測試
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CTRL	Control / Contrôle / Kontrolle / Controllo / Control / Controlo / Kontrolle / Μάρτυρας / 质控品 / Kontrolinė / Kontroll / Kontrola / Kontrola / Kontrola / 정도관리 / Kontrol / Контроль / Контролна / 質控品
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