ARCHITECT Cortisol

REF 8D15-25
REF 8D15-35

en
Cortisol
8D15
G1-0454/R08
B8D150

Read Highlighted Changes: Revised November 2015.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

NAME

ARCHITECT Cortisol

INTENDED USE

ARCHITECT Cortisol is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of cortisol in human serum, plasma or urine on the ARCHITECT iSystem. The ARCHITECT Cortisol assay is intended for use as an aid in the diagnosis and treatment of adrenal disorders.

SUMMARY AND EXPLANATION OF THE TEST

Cortisol is the major glucocorticoid hormone secreted by the adrenal cortex. Its physiological functions include regulation of carbohydrate metabolism and electrolyte and water distribution. Cortisol also has immunosuppressive and anti-inflammatory activity. In normal individuals, cortisol levels are regulated through a negative feedback loop in which the adrenal cortex responds to increased adrenocorticotropic hormone (ACTH) levels by increasing cortisol secretion, and the pituitary responds to elevated cortisol levels by down-regulation of ACTH production. Plasma cortisol levels are highest in the morning, and concentrations decrease by about half toward evening.[1] Pregnancy or estrogen treatment markedly elevates cortisol levels. Other stimuli such as severe stress may also lead to increased cortisol production.

Cortisol measurements are used as a direct monitor of adrenal status and an indirect measure of pituitary hyper or hypofunction. Elevated cortisol levels are associated with adrenal tumors, pituitary tumors or ectopic ACTH-producing tumors.[2] Subnormal cortisol concentrations may indicate generalized adrenal hypofunction or a defect in the metabolic pathway for cortisol biosynthesis.[3] The majority of cortisol in plasma is bound to proteins and approximately 1% is excreted unchanged into the urine.[4] Urinary cortisol is generally thought to reflect the level of unbound (free) plasma cortisol, which is biologically active. In cases of cortisol overproduction, cortisol-binding globulin becomes saturated, such that unbound plasma cortisol increases disproportionately, as does urinary excretion. The measurement of urinary cortisol is a sensitive means of determining adrenocortical hyperfunction such as Cushing's syndrome.[5, 6] Urinary cortisol from 24-hour collections represent integration over a full day and are not affected by the diurnal variation evident in plasma cortisol levels.

Cortisol measurements are often performed in conjunction with certain "challenge" tests designed to measure whether regulation of the hypothalamic-pituitary-adrenal axis is intact. These include the dexamethasone suppression test (DST), ACTH stimulation test and insulin tolerance test.[7-11] Such challenge tests aid in the differential diagnosis of Cushing's syndrome (cortisol overproduction) and the assessment of Addison's disease (cortisol underproduction).

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Cortisol assay is a delayed one-step immunoassay for the quantitative determination of cortisol in human serum, plasma or urine using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-cortisol coated paramagnetic microparticles are combined. The cortisol present in the sample binds to the anti-cortisol coated microparticles.
2. After incubation, cortisol acridinium-labeled conjugate is added to the reaction mixture.
3. Following a second incubation, the microparticles are washed, and pre-trigger and trigger solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is an inverse relationship between the amount of cortisol in the sample and the RLUs detected by the ARCHITECT iSystem optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT Cortisol 8D15

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT iSystems. Please contact your local distributor.

REF	8D15-25	8D15-35
Σ	100	500
MICROPARTICLES	1 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	1 x 26.3 mL

MICROPARTICLES Anti-cortisol (mouse, monoclonal) coated microparticles in TRIS/BIS-TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.09% solids. Preservatives: sodium azide and ProClin 300.

CONJUGATE Cortisol acridinium-labeled conjugate in citrate buffer with surfactant stabilizer. Minimum concentration: 0.7 ng/mL. Preservative: ProClin 300.

Other Reagents

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[12-15]

The following warnings and precautions apply to: MICROPARTICLES	
	
WARNING	Contains methylisothiazolones and sodium azide.
H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: CONJUGATE	
	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT Cortisol assay file must be installed on the ARCHITECT iSystem prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default result unit	Conversion factor	Alternate result unit
µg/dL	27.59[16]	nmol/L
	0.02759	µmol/L

- Conversion Formula: (Concentration in µg/dL) x (27.59) = nmol/L
- Conversion Formula: (Concentration in µg/dL) x (0.02759) = µmol/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Serum	Serum Serum separator tubes
Plasma	Lithium Heparin Plasma separator tubes with Lithium Heparin Sodium Heparin Potassium EDTA
Urine	Human urine may be used in the ARCHITECT Cortisol assay. The urine sample must be collected in a clean, previously unused container. Preservatives are not required; however, ten grams of boric acid per liter of urine may be used.

- Other anticoagulants have not been tested for use with the ARCHITECT Cortisol assay. Follow the manufacturer's processing instructions for collection tubes.
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum/plasma/urine.
- Other specimen collection tube types have not been tested with this assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - obvious microbial contamination
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for specimen collection tubes.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, centrifuge specimens before testing if
  - they contain fibrin, red blood cells, or other particulate matter
  - they were frozen and thawed or
  - appear cloudy
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma/Urine	2-8°C	≤ 14 days*
	-10°C or colder	≤ 30 days

*If testing will be delayed for more than eight hours, remove plasma or serum from the serum or plasma separator, red blood cells or clot.

Specimens removed from the separator gel, cells or clot may be stored up to 14 days at 2-8°C.

Urine samples may be stored up to 14 days at 2-8°C.

Serum, plasma or urine specimens can be stored up to 30 days at -10°C or colder.

Avoid multiple freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

8D15 ARCHITECT Cortisol Reagent Kit

Materials Required but not Provided

- ARCHITECT Cortisol Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 8D15-02 ARCHITECT Cortisol Calibrators
- Commercial controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**

- Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
- **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.

- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 70 µL

    Sample volume for each additional test from same sample cup: 20 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 20 µL
  - > 3 hours on board: Additional sample volume required.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT Cortisol Calibrators and Controls. Calibrators and Controls should be prepared according to their respective package inserts.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 5 drops

    for each control: 150 µL
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with a cortisol value exceeding 59.8 µg/dL are flagged with the code "> 59.8" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:2 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result. Specimens with a cortisol value exceeding 119.6 µg/dL are flagged with the code ">119.6" when run using the Automated Dilution Protocol. These specimens may be diluted by following the Manual Dilution Procedure.

Manual Dilution Procedure

Suggested dilution: 1:4

Prior to diluting the specimen, dispense approximately 7 drops of ARCHITECT Cortisol Calibrator A into a clean test tube for use in the next step.

1. Add 150 µL of ARCHITECT Cortisol Calibrator A from the test tube prepared in the prior step into another clean test tube and add 50 µL of the patient specimen.
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result should be > 3.0 µg/dL before the dilution factor is applied.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test Calibrators A, B, C, D, E, and F in duplicate. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0.0 - 59.8 µg/dL.
- Once an ARCHITECT Cortisol calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT Cortisol assay is that a single sample of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Each laboratory should establish control ranges to monitor the acceptable performance of the assay. If a control is out of its specified range, the associated sample results are invalid and the samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT Cortisol assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT Cortisol assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- Due to the diurnal variation of cortisol levels in normal subjects, all serum/plasma cortisol measurements should be referenced to the time of day of sample collection.
- Patients receiving fludrocortisone, prednisolone or prednisone (which is converted to prednisolone *in vivo*) may show artificially elevated cortisol values due to cross-reactivity. Cross-reactivity to endogenous and synthetic steroids is reported in the **SPECIFIC PERFORMANCE CHARACTERISTICS, Specificity** section in this package insert.
- If the cortisol results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).[17] Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies.[17, 18] Assay results that are not consistent with other clinical observations may require additional information for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[19] The presence of heterophilic antibodies in a patient specimen may cause anomalous values to be observed.[19] Additional information may be required for diagnosis.
- The concentration of cortisol in a given specimen, determined with assays from different manufacturers, can vary due to differences in assay methods, calibration, and reagent specificity.

EXPECTED VALUES

Reference Range: Serum

Serum cortisol levels were determined by assaying samples drawn from apparently healthy individuals collected before 10 a.m. and collected after 5 p.m. The 95% reference interval of the a.m. and p.m. populations was determined. Data from this study are summarized in the following table.*

Specimen Type	Specimen Collection	n	95% Reference Interval µg/dL	95% Reference Interval nmol/L
Serum	Before 10 a.m.	150	3.7 - 19.4	101.2 - 535.7
Serum	After 5 p.m.	150	2.9 - 17.3	79.0 - 477.8

* Representative data; results in individual laboratories may vary from these data. It is recommended that each laboratory establish its own reference range.

Reference Range: Urine

Cortisol levels in urine were determined by assaying 24-hour urine samples from apparently healthy individuals. The 95% reference interval was determined. Data from this study are summarized in the following table.*

Specimen Type	n	95% Reference Interval µg/24 hour[a]	95% Reference Interval nmol/24 hour[b]
Urine	128	4.3 - 176.0	11.8 - 485.6

[a] µg/24 hour = (Concentration in µg/dL) x (10) x (Volume of urine excreted in liters per 24 hours)

[b] nmol/24 hour = (Concentration in nmol/L) x (Volume of urine excreted in liters per 24 hours)

* Representative data; results in individual laboratories may vary from these data. It is recommended that each laboratory establish its own reference range.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Cortisol assay is designed to have an assay precision of ≤ 10% total CV for serum samples ≥ 3 to ≤ 35 µg/dL and ≤ 20% total CV for urine samples ≥ 3 to ≤ 35 µg/dL.

A study was performed with guidance from the National Committee for Clinical Laboratory Standards (NCCLS) document EP5-A2.[20] Abbott Immunoassay Multi-Constituent Controls (Levels 1, 2 and 3) and seven panels were assayed using two lots of reagents in replicates of two at two separate times per day for 20 days on two instruments. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized in the following table.*

Sample	Instrument	Reagent Lot	n	Mean Conc. (µg/dL)	Within Run SD	Within Run %CV	Total SD	Total %CV
Level 1	1	A	80	3.8	0.14	3.6	0.19	5.0
	2	B	80	4.0	0.19	4.8	0.23	5.8
Level 2	1	A	80	16.6	0.43	2.6	0.62	3.7
	2	B	80	17.3	0.40	2.3	1.32	7.7
Level 3	1	A	80	30.3	0.87	2.9	1.17	3.9
	2	B	80	31.0	0.63	2.1	1.32	4.3
Serum Panel 1	1	A	80	2.9	0.08	2.9	0.11	4.0
	2	B	80	2.9	0.16	5.5	0.18	6.2
Serum Panel 2	1	A	80	39.8	0.95	2.4	1.01	2.5
	2	B	80	41.0	1.08	2.6	1.29	3.2
Serum Panel 3	1	A	80	53.3	1.71	3.2	1.73	3.3
	2	B	80	55.8	1.50	2.7	1.87	3.4
Urine Panel 1	1	A	80	2.4	0.13	5.3	0.15	6.2
	2	B	80	2.7	0.16	6.1	0.17	6.4
Urine Panel 2	1	A	80	14.5	0.39	2.7	0.59	4.1
	2	B	80	15.9	0.60	3.8	0.72	4.5
Urine Panel 3	1	A	80	36.8	1.05	2.9	1.39	3.8
	2	B	80	40.6	1.56	3.9	1.59	3.9
Urine Panel 4	1	A	80	49.0	2.84	5.8	2.84	5.8
	2	B	80	53.7	3.18	5.9	3.18	5.9

* Representative data; results in individual laboratories may vary from these data.

Sensitivity

Functional Sensitivity

The ARCHITECT Cortisol assay is designed to have a functional sensitivity of ≤ 1 µg/dL.

In a study, serum and urine panels ranging in concentration from 0.1 - 2.1 µg/dL were tested in replicates of two over 10 days on two instruments using two reagent lots and two calibrations for a total of 40 replicates per panel. The total %CVs were calculated and plotted against the mean concentration. A reciprocal curve was fitted through the data and the functional sensitivity value was calculated as the concentration corresponding to the 20% CV level of the fitted curve. At the upper 95% confidence limit, the lowest ARCHITECT Cortisol assay value exhibiting a 20% CV was calculated to be 0.8 µg/dL for serum samples and 1 µg/dL for urine samples.*

* Representative data; results in individual laboratories may vary from these data.

Limit of Detection

The ARCHITECT Cortisol assay is designed to have a limit of detection (LoD) of ≤ 0.8 µg/dL. The limit of blank (LoB) and LoD of the ARCHITECT Cortisol assay were determined with guidance from NCCLS document EP17-A[21] using proportions of false positives (α) less than 5% and false negatives (β) less than 5%. These determinations were performed using 60 blank and 120 low level samples; LoB = 0.23 µg/dL and LoD = 0.40 µg/dL.*

* Representative data; results in individual laboratories may vary from these data.

Linearity

The ARCHITECT Cortisol assay is linear between 1 and 59.8 µg/dL based on a study performed with guidance from NCCLS document EP6-A.[22]

Specificity

The specificity of the ARCHITECT Cortisol assay was determined by studying the cross-reactivity of compounds whose chemical structure or concurrent usage may potentially interfere with the ARCHITECT Cortisol assay. Specificity of the assay was determined by spiking each compound into human serum specimens with cortisol levels spiked between 11.4 and 12.0 µg/dL.*

Compound	Concentration (µg/dL)	% Cross Reactivity
Aldosterone	1000	0.0
Beclomethasone	1000	0.0
Budesonide	1000	0.0
Canrenone	1000	0.1
Corticosterone	1000	0.9
Cortisol 21-glucuronide	1000	0.2
Cortisone	1000	2.7
β-Cortol	1000	0.0
β-Cortolone	1000	0.0
11-Deoxycorticosterone	100	0.0
11-Deoxycortisol	100	1.9
Dexamethasone	1000	0.0
DHEA	1000	0.0
DHEA-S	1000	0.0
β-Estradiol	1000	0.0
Estriol	1000	0.0
Estrone	1000	0.0
Fludrocortisone	100	36.6
Fluticasone Propionate	1000	0.0
6β-Hydroxycortisol	1000	0.2
17α-Hydroxypregnenolone	1000	0.1
11β-Hydroxyprogesterone	1000	0.2
17-Hydroxyprogesterone	1000	0.6
Medroxyprogesterone Acetate	1000	0.0
6-Methylprednisolone	1000	0.1
Mometasone	1000	0.0
Prednisolone	100	12.3
Prednisone	1000	0.6
Pregnanediol	1000	0.0
Pregnanetriol	1000	0.0
Pregnenolone	1000	0.0
Progesterone	1000	0.0
β-Sitosterol	1000	0.0
Spironolactone	1000	0.0
Testosterone	1000	0.0
Tetracycline	1000	0.0
Tetrahydrocortisol	1000	0.5
Triamcinolone	1000	0.5

* Representative data; results in individual laboratories may vary from these data.

Interference

Potential interference in the ARCHITECT Cortisol assay from the following compounds is designed to be ≤ 15% at the levels indicated. A study based on guidance from the CLSI Protocol EP7-A2[23] was performed for the ARCHITECT Cortisol assay. Serum specimens with cortisol levels between 5.1 and 34.2 µg/dL and urine specimens with cortisol levels between 4.6 and 37.9 µg/dL were supplemented with the following potentially interfering compounds. The average amount of interference observed during the study ranged from -7.8% to 13.2%.*

Specimen Type	Potentially Interfering Substance	Potentially Interfering Substance Concentration
Serum	Bilirubin	20 mg/dL
	Hemoglobin	500 mg/dL
	Total Protein (Low)	3 g/dL
	Total Protein (High)	10 g/dL
	Triglycerides	2000 mg/dL
Urine	Creatinine	5 mmol/L
	Urea	350 mmol/L
	Glucose	5 mmol/L
	Sodium Chloride	1000 mmol/L
	Total Protein (High)	1000 mg/dL

* Representative data; results in individual laboratories may vary from these data.

Evaluation of Other Potential Interferents

Potential interference in the ARCHITECT Cortisol assay from HAMA and rheumatoid factor (RF) is designed to be ≤ 15%. In a study, the ARCHITECT Cortisol assay was evaluated by testing specimens with HAMA and RF to further assess the clinical specificity. Specimens positive for HAMA and specimens positive for RF were evaluated for % interference with cortisol levels spiked between 9.0 and 44.1 µg/dL. Mean absolute % interference is summarized in the following table.*

Other Potential Interferents	n	Mean Absolute % Interference
HAMA Positive	10	1.0
RF Positive	10	5.9

* Representative data; results in individual laboratories may vary from these data.

Correlation

The ARCHITECT Cortisol assay is designed to have a slope of 1.0 ± 0.1 and a correlation coefficient (r) of ≥ 0.95 for serum samples when compared to Liquid Chromatography Mass Spectrometry/Mass Spectrometry (LCMS/ MS). The ARCHITECT Cortisol assay is also designed to have a slope of 1.0 ± 0.2 and a correlation coefficient (r) of ≥ 0.85 for urine samples when compared to LC-MS/MS. In a study the ARCHITECT Cortisol assay was compared to LC-MS/MS. Data from this study were analyzed using the Passing-Bablok[a] regression method and are summarized in the following table.*

ARCHITECT Cortisol vs. LC-MS/MS				
Specimen Type	n	Slope	Intercept	Correlation Coefficient (r)
Serum	125	1.08	-0.02	0.996
Urine	81	1.06	0.84	0.997

Serum Sample Range (ARCHITECT): 1.5 – 52.5 µg/dL

Serum Sample Range (LC-MS/MS): 1.4 – 49.4 µg/dL

Urine Sample Range (ARCHITECT): 0.8 – 51.1 µg/dL

Urine Sample Range (LC-MS/MS): 0.1 – 49.5 µg/dL

The ARCHITECT Cortisol assay is designed to have a correlation coefficient (r) of ≥ 0.90 for serum samples and ≥ 0.80 for urine samples when compared to the AxSYM Cortisol assay. In a study the ARCHITECT Cortisol assay was compared to the AxSYM Cortisol assay. Data from this study were analyzed using the Passing-Bablok[a] regression method and are summarized in the following table.*

ARCHITECT Cortisol vs. AxSYM Cortisol				
Specimen Type	n	Slope	Intercept	Correlation Coefficient (r)
Serum	121	0.91	0.92	0.983
Urine	74	0.54	-1.14	0.980

Serum Sample Range (ARCHITECT): 1.5 – 52.5 µg/dL

Serum Sample Range (AxSYM): 1.3 – 59.1 µg/dL

Urine Sample Range (ARCHITECT): 0.8 – 46.8 µg/dL

Urine Sample Range (AxSYM): 2.1 – 60.0 µg/dL

[a] A linear regression method with no special assumptions regarding the distribution of the samples and measurement errors.[24]

* Representative data; results in individual laboratories may vary from these data.

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
EC REP	Authorized Representative in the European Community
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF USA	Product of USA
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

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