ARCHITECT SHBG

REF 8K26-27
REF 8K26-21

en
SHBG
8K26
G95323R02
B8K2T0

Revised April 2018.

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 SHBG

INTENDED USE

The ARCHITECT SHBG assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of sex hormone binding globulin (SHBG) in human serum and plasma on the ARCHITECT iSystem.

The ARCHITECT SHBG assay is used as an aid in the diagnosis of androgen disorders.

SUMMARY AND EXPLANATION OF THE TEST

Sex hormone binding globulin (SHBG) is a glycoprotein of about 80-100 kDa; it has a high affinity for 17 beta-hydroxysteroid hormones such as testosterone and estradiol. SHBG concentration in plasma is regulated by, amongst other things, androgen/estrogen balance, thyroid hormones, insulin and dietary factors. It is the most important transport protein for estrogens and androgens in peripheral blood. SHBG concentration is a major factor regulating their distribution between the protein-bound and free states. Plasma SHBG concentrations are affected by a number of different diseases, high values being found in hyperthyroidism, hypogonadism, androgen insensitivity and hepatic cirrhosis in men. Low concentrations are found in myxoedema, hyperprolactinaemia and syndromes of excessive androgen activity. Measurement of SHBG is useful in the evaluation of mild disorders of androgen metabolism and enables identification of those women with hirsutism who are more likely to respond to estrogen therapy.

The ratio of testosterone to SHBG is also known as the Free Androgen Index (FAI) or the Free Testosterone Index (FTI). This ratio correlates well with both measured and calculated values of free testosterone and helps to discriminate subjects with excessive androgen activity from normal individuals.[1-3]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT SHBG assay is a two-step immunoassay to determine the presence of SHBG in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, assay diluent, and anti-SHBG coated paramagnetic microparticles are combined. The SHBG present in the sample binds to the anti-SHBG coated microparticles.
2. After washing, SHBG binds to the anti-SHBG acridinium-labeled conjugate that is added to create a reaction mixture.
3. Following another wash cycle, 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 a direct relationship between the amount of SHBG in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The concentration of SHBG in the sample is determined by comparing the chemiluminescent signal in the reaction to the ARCHITECT SHBG calibration.

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

REAGENTS

Kit Contents

ARCHITECT SHBG 8K26

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

REF	8K26-27	8K26-21
Σ	100	400
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL
ASSAY DILUENT	1 x 8.0 mL	4 x 8.0 mL

MICROPARTICLES Anti-SHBG (mouse, monoclonal) coated microparticles in TRIS buffer. Minimum concentration: 0.05% solids. Preservative: sodium azide.

CONJUGATE Anti-SHBG (mouse, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (mouse, bovine) stabilizers. Preservative: sodium azide.

ASSAY DILUENT SHBG Assay Diluent containing phosphate buffer with protein (mouse, bovine) stabilizers. Preservative: sodium azide.

Other Reagents

MULTI-ASSAY MANUAL DILUENT 1 x 100 mL ARCHITECT Multi-Assay Manual Diluent, REF 7D82-50, containing phosphate buffered saline solution. Preservative: antimicrobial agent.

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.[4-7]

The following warnings and precautions apply to: MICROPARTICLES / CONJUGATE / ASSAY DILUENT	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
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 SHBG assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM 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
nmol/L	0.095	µg/mL
	0.095	mg/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum Serum separator tubes
Human plasma	Lithium Heparin Sodium Heparin Ammonium Heparin

- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum or plasma.
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- 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.
- Potassium EDTA plasma can not be used with the ARCHITECT SHBG assay. SHBG dimer destabilization in EDTA could result in low SHBG measurements by immunoassay.[8] Use of Potassium EDTA tubes may result in a decrease in concentration values of greater than 20% when compared with serum collected in serum tubes.
- Na-Fluoride/K-Oxalate and Na-Citrate plasma separator tubes can not be used with the ARCHITECT SHBG assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed (> 500 mg/dL hemoglobin)
  - 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 collection tubes. Gravity separation is not sufficient for specimen preparation.
- 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, specimens must be transferred to a centrifuge tube and centrifuged at ≥ 10,000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
  - they contain fibrin, red blood cells, or other particulate matter, or
  - they require repeat testing.
- 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	2-8°C	≤ 8 days

Serum specimens may be stored at 2-8°C on or off the clot, red blood cells, or separator gel for ≤ 8 days.

Plasma specimens may be stored at 2-8°C on the clot, red blood cells, or separator gel for ≤ 8 days. Plasma specimens may be stored at 2-8°C off the clot, red blood cells, or separator gel for ≤ 5 days.

If testing will be delayed more than 8 days, remove serum or plasma from the clot, red blood cells, or separator gel and store frozen.

Serum and plasma specimens stored frozen for 3 months showed no performance differences.

Avoid more than 1 freeze/thaw cycle.

Plasma specimens may increase in concentration after one freeze/thaw cycle.

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

8K26 ARCHITECT SHBG Reagent Kit

Materials Required but not Provided

- ARCHITECT SHBG Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 8K26-02 ARCHITECT SHBG Calibrators
- 8K26-11 ARCHITECT SHBG Controls
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- 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. For additional information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT SHBG Calibrators and Controls.
  - Prior to use, thaw completely according to the respective calibrator and control package inserts.
  - Mix calibrator(s) and controls thoroughly by inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 6 drops

    for each control: 6 drops
- 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 an SHBG concentration of > 250 nmol/L will be flagged as ">250 nmol/L" and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:5 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Manual Dilution Procedure

Suggested dilution: 1:5

1. Add 30 µL of the patient specimen to 120 µL of ARCHITECT Multi-Assay Manual Diluent.
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 > 0.1 nmol/L 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-F in replicates of two. 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 – 250.0 nmol/L.
- Once an ARCHITECT SHBG 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 SHBG 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.

The ARCHITECT SHBG Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and 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 SHBG assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT SHBG 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

- Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.
- If the SHBG results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT SHBG) that employ mouse monoclonal antibodies.[9, 10]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis.[11]
- High protein concentration on plasma samples interferes with the ARCHITECT SHBG assay.

EXPECTED VALUES

It is recommended that each laboratory establish its own reference range, which may be unique to the population it serves depending on the geographical, dietary, or environmental factors. A reference range study was conducted with USA population, testing a total of 152 samples from female individuals and a total of 167 samples from male individuals. These samples gave the values summarized in the following table.*

		SHBG (nmol/L)		
	n	Median	2.5th percentile	97.5th percentile
Males	167	30.4	11.2	78.1
Females	152	48.2	11.7	137.2

A second reference range study was conducted with European population, testing a total of 200 samples from female individuals and a total of 224 samples from male individuals. These samples gave the values summarized in the following table.*

		SHBG (nmol/L)		
	n	Median	2.5th percentile	97.5th percentile
Males	224	34.8	13.5	71.4
Females	200	61.3	19.8	155.2

A third study was conducted testing a total of 113 samples from female individuals and a total of 111 samples from male individuals at two sites. The free testosterone index (% FTI) or free androgen index (% FAI) correlates with the value of free testosterone.[2] Therefore, in addition to SHBG all samples were tested with ARCHITECT Testosterone. The free testosterone index (% FTI) or free androgen index (% FAI) was calculated on a molar/molar basis. These samples gave values for the different groups summarized in the following table.*

SHBG and Total Testosterone

		SHBG (nmol/L)			Testosterone (ng/mL)[a]		
	n	Median	5th perc.	95th perc.	Median	5th perc.	95th perc.
Normal Men	111	39.7	17.1	77.6	4.86	2.54	8.53
Premenopausal women	59	88.9	34.3	147.7	0.58	0.16	1.17
Postmenopausal women	54	57.2	26.4	118.0	0.45	0.16	1.00

Free Testosterone Index or Free Androgen Index

		FTI or FAI (%)[b]		
	n	Median	5th percentile	95th percentile
Normal Men	111	41.7	20.4	81.2
Premenopausal women	59	2.5	0.5	7.3
Postmenopausal women	54	2.5	0.6	8.0

[a] The default unit for the ARCHITECT Testosterone assay is ng/mL.

- When the alternate result unit, nmol/L, is selected, the conversion factor used by the system is 3.47.
  Conversion formula: [concentration in ng/mL] x 3.47= nmol/L

[b] $\text{FTI (\%)} = \frac{\text{Testosterone Value (nmol/L)}}{\text{SHBG Value (nmol/L)}} \times 100$

* Representative performance data are shown. Results obtained at individual laboratories may vary.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT SHBG assay is designed to have a precision of ≤ 10% total CV. A study was performed with the ARCHITECT SHBG assay based on guidance from the Clinical and Laboratory Standards Institute, document NCCLS Protocol EP5-A[12]. Multiple ARCHITECT SHBG control lots and three serum samples were assayed using one lot of reagents in replicates of two at two separate times per day for 20 days at one site and on one instrument. In addition, two lots of reagents were assayed for 10 days on three other instruments at different sites. A third reagent lot was tested in replicates of two at two separate times per day for 5 days on one instrument. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized in the following table.*

		Mean Conc.	Within Run		Total[a]	
Sample	n	(nmol/L)	SD	%CV	SD	%CV
Low Control	1640	8.8	0.42	4.78	0.84	9.54
Medium Control	1640	24.5	1.18	4.80	1.38	5.65
High Control	1640	152.8	8.00	5.24	11.53	7.55
Human Serum Low	760	16.8	0.86	5.11	1.11	6.63
Human Serum Medium	760	47.3	2.26	4.78	3.77	7.97
Human Serum High	760	146.2	7.48	5.11	13.10	8.96

[a] Total assay variability contains within run, run to run and day to day variability.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Recovery

The ARCHITECT SHBG assay is designed to have a mean recovery of 100 +/- 10%. A study was performed where known concentrations (12.5, 25, 50, 100, 200 nmol/L) of SHBG were added to 10 aliquots of human serum with endogenous levels ranging from 9.4 to 46.6 nmol/L. The concentration of SHBG and the percent recovery were calculated for each sample. The percent recovery of the ARCHITECT SHBG assay resulted in a mean of 99%. Data are representative performance data, but results obtained at individual laboratories may vary.

Dilution Linearity

The ARCHITECT SHBG assay is designed to recover diluted specimens within +/- 10% of the expected result. A dilution linearity study was performed using specimens with undiluted values that ranged between 30.0 and 158.2 nmol/L. These specimens were diluted manually using ARCHITECT Multi-Assay Manual Diluent at various dilution factors (0.2 to 0.9) to result in 80 to 10% of the endogenous SHBG level. Data from this study are summarized in the following tables.*

Sample	Dilution Factor	Observed Values (nmol/L)	% Mean Recovery[a]
1	undiluted	30.0	-
	0.2 to 0.9	24.3 - 3.1	100
2	undiluted	78.0	-
	0.2 to 0.9	57.4 - 7.7	98
3	undiluted	158.2	-
	0.2 to 0.9	124.2 - 15.1	97

In addition, a dilution study was performed using specimens with different high and low SHBG concentration values ranging between 24.7 to 214.0 nmol/L. The low level sample was used to dilute the high level sample to different concentrations (dilution factors of 0.25 to 0.75).

Sample Pair	Undiluted Concentration Level (nmol/L)	Diluted Concentration Range (nmol/L)	% Mean Recovery[a]
1	Low 26.3 High 214.0	67.0 to 165.6	96
2	Low 24.7 High 205.8	71.3 to 155.3	100
3	Low 26.5 High 163.8	65.2 to 132.5	103

[a] % Recovery = $\frac{\text{Observed Value (nmol/L)}}{\text{Expected Value (nmol/L)}} \times 100$

% Mean Recovery = Mean of % Recovery of all dilutions of a sample

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Sensitivity

The ARCHITECT SHBG assay is designed to have an analytical sensitivity of ≤ 0.1 nmol/L. Analytical sensitivity is defined as the concentration at two standard deviations above the calibrator A (0.0 nmol/L). In a study (n = 6 runs, 20 replicates of calibrator A using three instruments and two reagent lots), the analytical sensitivity was calculated to be 0.02 nmol/L* at a 95% level of confidence.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Specificity

The specificity of the ARCHITECT SHBG assay is designed to have no detectable cross-reactivity when tested with structurally similar compounds listed in the table below. A study was performed with the ARCHITECT SHBG assay based on guidance from the Clinical and Laboratory Standards Institute, document NCCLS Protocol EP7-A.[13] Aliquots of calibrator A, containing essentially no residual SHBG, were supplemented with potential cross-reactants at the concentrations listed and tested for SHBG. Data from this study are summarized in the following table.*

Compound	Concentration Cross-Reactant	% Cross Reactivity[a]
AFP	400 ng/mL	0.00
Cortisol	100,000 ng/mL	0.00
11-Deoxycortisol	4,000 ng/mL	0.00
Estradiol	3,600 pg/mL	0.00
Testosterone	20,000 ng/mL	0.00
5-dihydrotestosterone	20,000 ng/mL	0.00
TG	300 ng/mL	0.00
TBG	200 µg/mL	0.00
Transferrin	4 mg/mL	0.00

[a] % Cross-Reactivity = $\frac{\text{Mean Value spiked - Mean Value non spiked (nmol/L)}}{\text{Concentration of Cross-Reactant (nmol/L)}} \times 100$

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Interference

Potential interference in the ARCHITECT SHBG assay from hemoglobin, bilirubin, triglycerides, and protein at the levels indicated below is designed to be ≤ 10%. Interference was demonstrated by a study based on guidance from the Clinical and Laboratory Standards Institute, document NCCLS Protocol EP7-A.[13] There was no significant interference observed since the % mean recovery is within +/- 10% of the expected value. Data from this study are summarized in the following table.*

Potentially Interfering Substance	Concentration	% Mean Recovery[a]
Hemoglobin	500 mg/dL	99
Bilirubin	20 mg/dL	99
Triglycerides	4000 mg/dL	103
Protein low	4 g/dL	104
Protein high	12 g/dL	95[b]

[a] % Recovery = $\frac{\text{Observed Value (nmol/L)}}{\text{Expected Value (nmol/L)}} \times 100$

% Mean Recovery = Mean of % Recovery of all tested serum and plasma samples.

[b] Data provided for high protein are based on serum samples. High protein concentration on plasma samples interferes with the ARCHITECT SHBG assay.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Method Comparison

The ARCHITECT SHBG assay is designed to have a slope difference of +/- 15% and a correlation coefficient of ≥ 0.90 when compared to a commercially available diagnostic kit. A study was performed with the ARCHITECT SHBG assay, where regression analysis was performed using the Passing-Bablok and Least Squares regression methods. Data from this study are summarized in the following table and graph.*

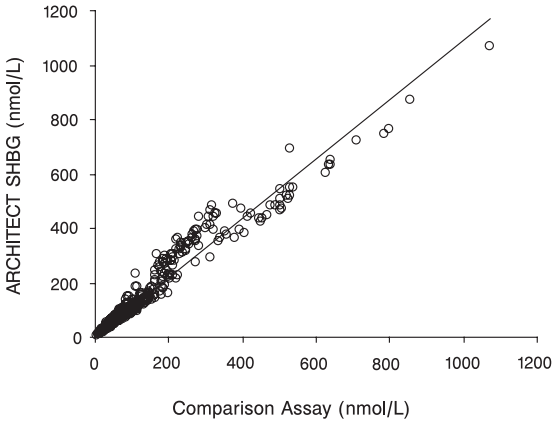
In this evaluation, specimen concentrations range from 5.7 nmol/L to 1067.6 nmol/L with the ARCHITECT SHBG assay and from 6.5 nmol/L to 1072.0 nmol/L with the commercially available diagnostic kit. This evaluation also includes specimens diluted by the instrument.

ARCHITECT SHBG vs. Comparison Assay

Regression Method	n	Slope	Intercept	Correlation Coefficient
Passing-Bablok [a]	626	1.09	0.35	0.98
Least Squares	626	1.07	7.11	

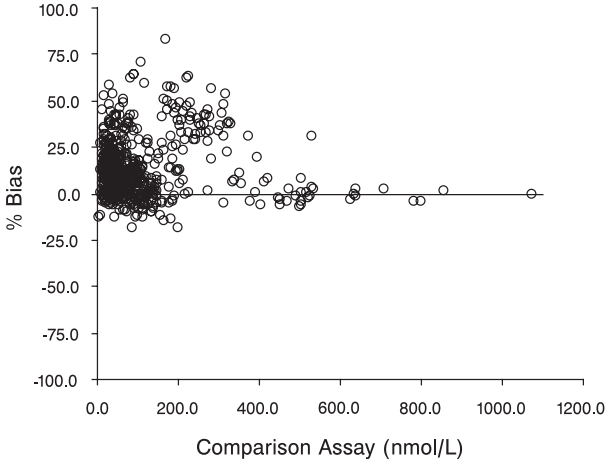
[a] A linear regression method with no special assumptions regarding the distribution of samples and measurement errors.[14]

ARCHITECT SHBG vs. Comparison Assay



A bias analysis of the ARCHITECT SHBG vs. the comparison assay was performed on the same 626[b] serum specimens in the range of 5.7 to 1072.0 nmol/L. The average % Bias of ARCHITECT SHBG vs. the comparison assay in this study was 13.26%. The 95% confidence interval of that average percent bias is -19.87% to 46.38%. The following graph demonstrates the % Bias between the two assays.*

ARCHITECT SHBG % Bias to Comparison Assay



[b] One data point was removed for presentation purposes. The % Bias between the two assays for this data point was 113.7%. The concentration was 231.7 nmol/L on ARCHITECT SHBG and 108.4 nmol/L on the comparison assay.

* Representative performance data are shown. Variables such as differences in sampling size and sample population may impact the correlation of the assay, therefore, results obtained at 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
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF SPAIN	Product of Spain
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
WASH BUFFER	Wash Buffer

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