ARCHITECT

SYSTEM

CE

**SHBG**

IVD REF 8K26

**34-7077/R4**

# SHBG

**Customer Service**
**United States: 1-877-4ABBOTT**
**International: Call your Abbott representative**

This package insert must be read carefully before product use. 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.

**Read Highlighted Changes**
**Revised September 2007**

## Key to symbols used

| | | | |
|---|---|---|---|
| REF | List Number | LOT | Lot Number |
| IVD | *In Vitro* Diagnostic Medical Device | | Expiration Date |
| | | REACTION VESSELS | Reaction Vessels |
| 2°C 8°C | Store at 2-8°C | SAMPLE CUPS | Sample Cups |
| | | SEPTUM | Septum |
| | Consult instructions for use | REPLACEMENT CAPS | Replacement Caps |
| SN | Serial Number | REAGENT LOT | Reagent Lot |
| | | ASSAY CD-ROM | Assay CD-ROM |
| | Manufacturer | CONTROL NO. | Control Number |

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

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

## SUMMARY AND EXPLANATION OF 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.[1,2,3]

## 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. In the first step, sample, assay diluent, and anti-SHBG coated paramagnetic microparticles are combined. SHBG present in the sample binds to anti-SHBG coated microparticles. After washing, the SHBG binds to the anti-SHBG acridinium-labeled conjugate that is added in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of SHBG in the sample and the RLUs detected by the ARCHITECT *i* System 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

### Reagent Kit, 100 Tests

NOTE: Some kit sizes are not available in all countries. Please contact your local distributor.

ARCHITECT SHBG Reagent Kit (8K26)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL each) Anti-SHBG (mouse, monoclonal) coated microparticles in TRIS buffer. Preservative: sodium azide.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL each) Anti-SHBG (mouse, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (mouse, bovine) stabilizers. Preservative: sodium azide.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (8.0 mL each) SHBG Assay Diluent containing phosphate buffer with protein (mouse, bovine) stabilizers. Preservative: sodium azide.

### Assay Diluent

ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50)

- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT *i* Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

### Other Reagents

ARCHITECT *i* Pre-Trigger Solution

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

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

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

## WARNINGS AND PRECAUTIONS

**For *In Vitro* Diagnostic Use.**

### Safety Precautions

- **CAUTION:** It is recommended that all human sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens.[4] Biosafety Level 2[5] or other appropriate biosafety practices[6,7] should be used for materials that contain or are suspected of containing infectious agents.
- All components contain sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

### Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Before loading the ARCHITECT SHBG Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that 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, which 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.

### Storage Instructions

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The ARCHITECT SHBG Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT SHBG Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

- Reagents may be stored on or off the ARCHITECT *i* System. 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.** After reagents are removed from the system, initiate a reagent scan to update the onboard stability timer.

### 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 *i* System from the ARCHITECT *i* Assay CD-ROM Addition E before performing the assay. For detailed information on assay file installation and on 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.
- The default result unit for the ARCHITECT SHBG assay is nmol/L. An alternate result unit, µg/mL or mg/L, may be selected for reporting results by editing assay parameter "Result concentration units" to µg/mL or mg/L. The conversion factor used by the system is 0.095.
  - Conversion formula:
    (Concentration in nmol/L) x (0.095) = µg/mL or mg/L.

## SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

### Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT SHBG assay.

- Human serum (including serum collected in serum separator tubes)
- Human plasma collected in:
  - Lithium Heparin
  - Sodium Heparin
  - Ammonium Heparin
  - Potassium EDTA
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System 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 ARCHITECT SHBG assay.
- 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)
  - obvious microbial contamination
  - cadaver specimen or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells or other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, 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.

### Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma 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 specimens to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimens without the lipemic material.

### Storage

- Specimens may be stored on the clot, red blood cells, or separator gel for up to 8 days refrigerated at 2-8°C.
- 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.

### Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped on wet ice or on dry ice. Do not exceed the storage time limitations listed above.

## PROCEDURE

### Materials Provided

- 8K26 ARCHITECT SHBG Reagent Kit

### Materials Required but not Provided

- ARCHITECT *i* System
- 1L65 ARCHITECT *i* **ASSAY CD-ROM** - US - Addition E
- 1L66 ARCHITECT *i* **ASSAY CD-ROM** - WW (excluding US) - Addition E
- 8K26-01 ARCHITECT SHBG Calibrators
- 8K26-10 ARCHITECT SHBG Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- 7D82 ARCHITECT *i* **MULTI-ASSAY MANUAL DILUENT**
- Pipettes or pipette tips (optional)

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

### Assay Procedure

- Before loading the ARCHITECT SHBG Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that 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 remain adhered to the bottle, continue inverting 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 on placing septums on bottles, refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT SHBG Reagent Kit on the ARCHITECT *i* System.
  - Verify that all necessary assay reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibration, 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.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
  - Priority: 70 µL for the first ARCHITECT SHBG test plus 20 µL for each additional ARCHITECT SHBG test from the same sample cup.
  - ≤ 3 hours on board: 150 µL for the first ARCHITECT SHBG test plus 20 µL for each additional ARCHITECT SHBG test from the same sample cup.
  - > 3 hours on board: additional sample volume is 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 calibrators and controls.
  - Prior to use, thaw completely according to the respective calibrator and control package inserts.
  - Mix ARCHITECT SHBG Calibrators and Controls thoroughly by inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT SHBG Calibrators and Controls, hold the bottles **vertically** and dispense 6 drops of each calibrator or 6 drops of each control into each respective sample cup.
- 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 Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those 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.

- If using the 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 dilutions should be performed as follows:
  - The suggested dilution for the ARCHITECT SHBG assay is 1:5.
  - Add 30 µL of the patient specimen to 120 µL of ARCHITECT *i* Multi-Assay Manual Diluent.
  - 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 (before dilution factor is applied) should be greater than 0.1 nmol/L.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

### Calibration

- To perform an ARCHITECT SHBG calibration, test calibrators A, B, C, D, E, and F in replicates of two. A single sample of each SHBG control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- 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.
  - 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 be tested once every 24 hours each day of use. If laboratory quality control procedures require more frequent use of controls to verify test results, follow those 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. ARCHITECT SHBG Calibrators may be used when MasterCheck is not available. Refer to the ARCHITECT System Operations Manual, Appendix B.

## RESULTS

### Calculation

The ARCHITECT SHBG assay uses a 4 Parameter Logistic Curve fit (4PLC, Y-weighted) data reduction method 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

- If the SHBG results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, the ARCHITECT SHBG assay 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).[8,9] Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT SHBG) that employ mouse monoclonal antibodies.[9]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[10] 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.
- 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[11]. 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 *i* 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<br>High 214.0 | 67.0<br>to 165.6 | 96 |
| 2 | Low 24.7<br>High 205.8 | 71.3<br>to 155.3 | 100 |
| 3 | Low 26.5<br>High 163.8 | 65.2<br>to 132.3 | 103 |

[a] % Recovery = $\frac{\text{Observed Value (nmol/L)}}{\text{Expected Value (nmol/L)}}$ x 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.[12] 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 = $\frac{\text{Mean Value spiked - Mean Value non spiked (nmol/L)}}{\text{Concentration of Cross-Reactant (nmol/L)}}$ x 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.[12] 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 = $\frac{\text{Observed Value (nmol/L)}}{\text{Expected Value (nmol/L)}}$ x 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

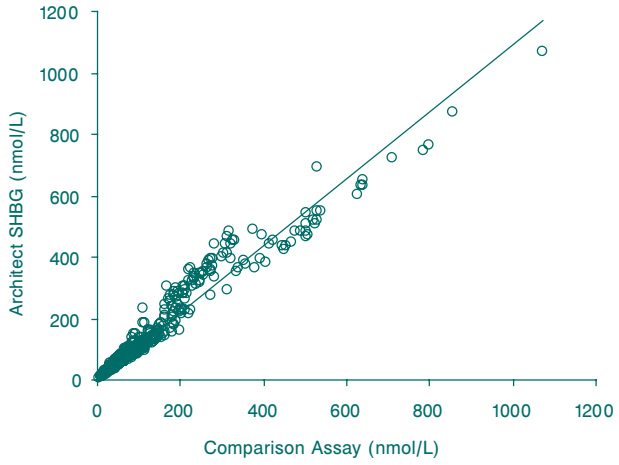
The ARCHITECT SHBG assay is designed to have a slope difference of +/- 15% and a correlation coefficient of ≥ 0.90 when compared to a commercially available diagnostic kit. A study was performed with the ARCHITECT SHBG assay, where regression analysis was performed using the Passing-Bablok and Least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

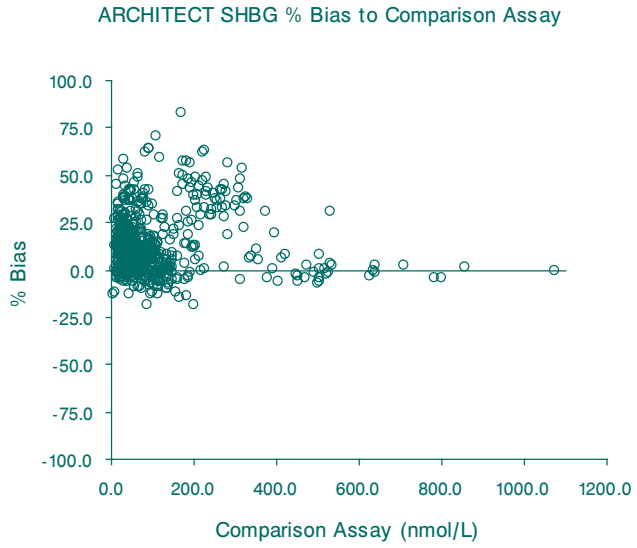
| Regression Method | n | Slope | Intercept | Correlation Coefficient |
|---|---|---|---|---|
| Passing-Bablok[a] | 626 | 1.09 | 0.35 | 0.98 |
| Least Squares | 626 | 1.07 | 7.11 | |

[a] A linear regression method with no special assumptions regarding the distribution of samples and measurement errors.[13]

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.*




[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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