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

Key to symbols used

- **REP**: List Number
- **LOT**: Lot Number
- **ST**: Store at 2-8°C
- **RE**: In Vitro Diagnostic Medical Device
- **SO**: Expiration Date
- **CAP**: Replacement Caps
- **REAG**: Reagent Lot
- **CT**: Consult Instructions for use
- **CD**: Assay CD-ROM
- **CN**: Authorized Representative
- **SN**: Control Number
- **CAU**: Manufacturer
- **LE**: Caution: Irritant

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

NAME
ARCHITECT / Digoxin

INTENDED USE
The ARCHITECT Digoxin assay is an in vitro chemiluminescent microplate immunoassay (CMI) for the quantitative measurement of digoxin in human serum or plasma on the ARCHITECT System with STAT protocol capability. The measurements obtained are used to aid in the diagnosis and treatment of digoxin overdose and in monitoring levels of digoxin to help ensure appropriate therapy.

SUMMARY AND EXPLANATION OF TEST
Digoxin is a potent cardiac glycoside prescribed for the treatment of patients suffering from congestive heart failure or from some types of cardiac arrhythmias. Monitoring of serum or plasma digoxin levels is important because the drug has a narrow therapeutic ratio (a small difference between therapeutic and tissue toxic levels) and because the symptoms of drug overdose may resemble the original condition for which the drug was prescribed. Also, digoxin dosage may require adjustment when renal function is impaired or when drugs known to alter the pharmacokinetics of digoxin (e.g., quinidine, verapamil, or amiodarone) are coadministered. Monitoring serum or plasma digoxin levels along with other clinical data can aid the physician in adjusting patient dosage to achieve optimal therapeutic effect while avoiding subtherapeutic or toxic dosage levels.

BIological PRINCIPLES OF THE PROCEDURE
The ARCHITECT Digoxin assay is a one-step STAT immunoassay for the quantitative measurement of digoxin in human serum or plasma using CMA technology with flexible assay protocols, referred to as ChemiFlex. Sample, anti-digoxin coated paramagnetic microparticles, assay diluent, and digoxigenin acridinium-labeled conjugate are combined to create a reaction mixture. The anti-digoxin coated microparticles bind to digoxin present in the sample and to the digoxigenin acridinium-labeled conjugate. After washing, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). An indirect relationship exists between the amount of digoxin in the sample and the RLUs detected by the ARCHITECT System.

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

REAGENTS
Reagent Kit, 100 Tests
Note: Some lot sizes are not available in all countries or for use on all ARCHITECT Systems. Please contact your local distributor.

ARCHITECT / Digoxin Reagent Kit (1P32)

• PRe-Trigger Solution

• Post-Trigger Solution

• Wash Buffer

• MicroParticles: 1 Bottle (16.7 mL), disk-digoxin (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizer. Preservatives: ProClin 300.

• Conjugate: 1 Bottle (5.9 mL), Digoxigenin acridinium-labeled conjugate. Preservatives: ProClin 300.

• Assay Diluent: 1 Bottle (10.0 mL), Assay Diluent containing goat serum with EDTA disodium. Preservatives: ProClin 300 and ProClin 950.

• Other Reagents

ARCHITECT / Pre-Trigger Solution

POST-TRIGGER SOLUTION (Pre-Trigger Solution containing 1.5% [w/v] hydrogen peroxide) 

ARCHITECT / Trigger Solution

DIGOXIN SOLUTION (Digoxin Solution containing 0.35 N sodium hydroxide)

ARCHITECT / Wash Buffer

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

WARNINGS AND PRECAUTIONS
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 CDC Guide to Bloodborne Pathogens. The measurements obtained are used to aid in the diagnosis and treatment of digoxin overdose and in monitoring levels of digoxin to help ensure appropriate therapy.

• Other safety considerations: 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 residual waste and for further information, refer to the ARCHITECT System Operations Manual, Section 6.

• Do not use reagents beyond the expiration date.

• Do not pool reagents within a kit or between reagent kits.

• Before loading the ARCHITECT Digoxin Reagent Kit on the system for the first time, the reagent bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the PROCEDURE, Procedure 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 unopened reagent bottle.

• 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 residual waste and for further information, refer to the ARCHITECT System Operations Manual, Section 6.

• Do not use reagents beyond the expiration date.

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• 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 unopened reagent bottle.

• Once a septum has been placed on the 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.
Storage Instructions

- The ARCHITECT Digoxin 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 Digoxin Reagent Kit may be stored on board the ARCHITECT System with STAT protocol capability 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 System. If reagents are removed from the system, they should be stored 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 shipping onboard time, 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 Digoxin assay file must be installed on the ARCHITECT System with STAT protocol capability from the ARCHITECT Assay CD-ROM, previous 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 Digoxin assay is ng/mL. An alternate result unit, mmol/L, may be selected for reporting results by editing assay parameter "Result concentration units" to mmol/L. The conversion formula used by the system is as follows:
  \[ \text{Concentration in mmol/L} = \frac{\text{Concentration in ng/mL}}{1.28} \]

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

- The following specimen tube types were verified for use with the ARCHITECT Digoxin assay. Other specimen collection tubes, including gel separation tubes, have not been tested with this assay.
  - Human serum
  - Human plasma collected in plain or sodium heparin
  - Plasma samples from different anticoagulant tube types should not be used interchangeably for monitoring digoxin.
  - Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
  - The ARCHITECT 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 Digoxin assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - Head-injured
  - Grossly hemolyzed (>750 mg/dL)
  - Obvious microcrystalline contamination
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum and plasma.

- 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.
- 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 before testing if they contain fibrin, red blood cells, or other particulate matter, they require repeat testing, or they were frozen and thawed.
- 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 specimen without the lipemic material.
- Transfer clarified specimen to a sample cup or secondary tube for testing.

Storage

- Serum or plasma should be separated from the clot or red blood cells as soon as collection as possible.
- Specimens removed from the clot or red blood cells may be stored for up to 48 hours at room temperature (15-30°C) or up to 48 hours at 4°C.
- Serum or plasma specimens can be stored at -20°C or colder for up to 6 months.
- Avoid more than 3 freeze/thaw cycles.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot or red blood cells.
- 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 dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 1P32 ARCHITECT Digoxin Reagent Kit

Materials Required but not Provided

- ARCHITECT System with STAT protocol capability
- 1LBR ARCHITECT System - Additions E
- 1LBR ARCHITECT System - Additions G, H
- 1P32-01 ARCHITECT Digoxin Calibrators
- 6E20-10 Abbott Immunoassay-MCC (Liquid) or other commercial controls
- ARCHITECT CALIBRATOR SALES SOLUTION
- ARCHITECT CALIBRATOR STANDARD SOLUTION
- ARCHITECT CALIBRATOR REPLACEMENT CAPS
- Pipettes or plastic-tipped (optimal) 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 ARCHITECT® Digoxin 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 Handling Precautions section of this package insert.

Load the ARCHITECT® Digoxin Reagent Kit on the ARCHITECT® System with JCIF protocol capability.
• 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.
• 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.
• For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.

Prepare calibrators and controls.
• Mix ARCHITECT® Digoxin Calibrators by gentle inversion before use.
• To obtain the recommended volume requirement for the ARCHITECT® Digoxin Calibrators, hold the bottles vertically and dispense 5 drops of each calibrator onto each respective sample cup.
• Dispense 150 μL of each control onto each respective sample cup.

Load samples.
• For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
• Press RIN.
• For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 5.
• For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 5. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures
• Serum or plasma specimens with a digoxin concentration ≥ 4.00 ng/mL will be flagged as ">4.00 ng/mL" and may be manually diluted.
• Manually dilute specimens (1:10) with Calibrator A. Add 20 μL of patient specimen to 180 μL of Calibrator A.
• 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 the dilution factor is applied should be greater than 0.30 ng/mL.
• For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration
• To perform a calibration, test the ARCHITECT® Digoxin Calibrators A to F in duplicate. The calibrators should be prior to loading.
• A single replicate of each control level must be tested to evaluate the assay calibration.

Order controls as described in the Assay Procedure section.
• Ensure that assay control values are within the ranges specified in the control package insert.
• Calibration range: 0.0 to 4.0 ng/mL.
• Once an ARCHITECT® Digoxin calibration is accepted and stored, all subsequent samples may be tested without further calibration unless one or both of the following occur:
  • A reagent kit with a new lot number is used
  • Controls are out of range

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT® Digoxin assay is that a single sample of each control level be tested once every 24 hours of each day. If laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

The 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 must be repeated. 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® Digoxin assay belongs to method group 2.

Use ARCHITECT® Digoxin Calibrators in place of MasterCheck as described in the ARCHITECT System Operations Manual, Appendix B.

RESULTS

Calculation

The ARCHITECT® Digoxin assay uses a 4 Parameter Logistic Curve Fit (PLC, 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.

Measurement Range (Reportable Range)

The measurement range for the ARCHITECT® Digoxin assay is defined as 0.3 to 4.0 ng/mL.

LIMITATIONS OF THE PROCEDURE

• If the ARCHITECT® Digoxin assay 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.
• Plasma samples from different anticoagulant tube types should not be used interchangeably for monitoring digoxin.
• Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).11,12 Such specimens may show erroneous values when tested with assay kits (such as ARCHITECT® Digoxin) that employ mouse monoclonal antibodies.11,12
• Some immunoassays for digoxin may cross-react with metabolites, which can lead to a positive bias in patient results. Refer to the SPECIFIC PERFORMANCE CHARACTERISTICS, Specificity section of this package insert for estimates of cross-reactivity of ARCHITECT® Digoxin to some metabolites of digoxin.
• Digoxin values for specimens from patients who have received DIGIBIND® or DIGIFAB® therapy may be impacted. See the SPECIFIC PERFORMANCE CHARACTERISTICS, Interfering Substances section.
states, concurrent medications, and other clinical factors. Refer to the factors to consider when evaluating the correct therapeutic dosage for cannot be made on the basis of digoxin concentrations alone. Most studies be realized at serum or plasma concentrations below 0.8 ng/mL. Symptoms of digoxin toxicity may include gastrointestinal disturbances such as anorexia, nausea, vomiting and diarrhea, central nervous system disturbances manifested by blurred or yellow vision, headache, weakness, dizziness, apathy, and confusion, and cardiac rhythm disturbances and tachycardias. There is some evidence that children may tolerate slightly higher serum or plasma concentrations than adults. It is important to note that the distinction between adequate digitalization and toxicity in patients cannot be made on the basis of digoxin concentrations alone. Most studies show a significant overlap between the toxic and nontoxic groups. Additional factors to consider when evaluating the correct therapeutic dosage for each patient are lean body weight, age, renal function, concurrent disease states, concurrent medications, and other clinical factors. Refer to the drug manufacturer’s package insert. Each laboratory should establish its own therapeutic (reference) range for digoxin.

SPECIFIC PERFORMANCE CHARACTERISTICS

Performance was evaluated on the ARCHITECT i2000SR System. Precision

The ARCHITECT i2000SR assay is designed to have an assay precision of ±10% total CV. A study was performed with guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP2-A2. Abbott Immunos flyer-MCC (Liquid) (Levels 1, 2, and 3) and three human serum panels were assayed in replicates of two at least two separate times per day for 20 days using two lots of reagents on two instruments. Each reagent lot used a single calibration curve throughout the study. The data are summarized in the following table.*

<table>
<thead>
<tr>
<th>Level</th>
<th>Sample Mean</th>
<th>CV %</th>
<th>SD %CV</th>
<th>Total SD %CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,204</td>
<td>1.73</td>
<td>0.06</td>
<td>1.76</td>
</tr>
<tr>
<td>2</td>
<td>1,204</td>
<td>1.73</td>
<td>0.06</td>
<td>1.76</td>
</tr>
<tr>
<td>3</td>
<td>1,204</td>
<td>1.73</td>
<td>0.06</td>
<td>1.76</td>
</tr>
</tbody>
</table>

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

Recovery

The ARCHITECT i2000SR assay is designed to have a grand mean recovery of 100 ± 10%.

A study was performed on five serum samples containing low levels of digoxin and each sample was spiked with additional digoxin at concentrations of 0.0, 0.5, 1.0, 2.0, and 3.0 ng/mL. The concentration of digoxin was determined using the ARCHITECT i2000SR assay and the resulting percent recovery was calculated. The individual percent recovery of the ARCHITECT i2000SR assay for serum ranged from 98.8% to 104.3%. The mean percent recovery of the ARCHITECT i2000SR assay for serum ranged from 94.9% to 103.9% with a grand mean for serum of 101.4%.*

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

Dilution Linearity

The ARCHITECT i2000SR assay is designed to have a mean deviation from linearity of a 10% for concentrations over 1.0 ng/mL, or ±0.1 ng/mL at concentrations less than 1.0 ng/mL. A dilution linearity study was performed by diluting five serum samples with ARCHITECT i2000SR Calibrator A. The concentration of digoxin was determined using the ARCHITECT i2000SR assay and the resulting percent deviation from linearity or concentration difference was calculated. For diluted samples reading above 1.0 ng/mL, the percent deviation from linearity ranged from -4.0 to 8.8% with a mean percent deviation from linearity of 2.0%. For diluted samples below 1.0 ng/mL, the concentrations were within 0.1 ng/mL of the expected results. The linear range of the assay is 0.3 to 4.0 ng/mL. * Representative data; results in individual laboratories may vary from these data. Sensitivity

The ARCHITECT i2000SR assay is designed to have a Limit of Detection of ≤0.3 ng/mL. Limit of Blot (LoB) and Limit of Detection (LoD)

The LoB and LoD of the ARCHITECT i2000SR assay were determined with guidance from CLSI Document EP17-A2 using proportions of false positives (α) less than 5% and false negatives (β) less than 5%. These determinations were performed using one blank (60 replicates) and four low level digoxin samples (15 replicates each); LoB = 0.07 ng/mL and LoD = 0.09 ng/mL.* * Representative data; results in individual laboratories may vary from these data.

Functional Sensitivity

In order to perform the Functional Sensitivity study, a series of serum samples ranging from 0.05 to 0.5 ng/mL, were prepared by diluting Calibrator B with Calibrator A. These samples were tested in replicates of ten two times per day for five days using one reagent and calibrator kit for a total of 100 replicates per panel. The total % CVs were calculated and plotted against the mean concentration. A rectilinear 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 i2000SR assay value yielding a 20% CV was calculated to be 0.1 ng/mL, which is below the reportable range of the ARCHITECT i2000SR assay.* * Representative data; results in individual laboratories may vary from these data.
Specificity

Cross-reactivity was tested for the major digoxin active metabolites (digoxigenin digoxigenin di-digitoxoside, digitoxin, and digoxin), related compounds (acetyldigoxin, digoxin digoxigenin, ouabain, deslanoside, lanatoside C, proscillaridin) and other therapeutic agents that may be coadministered to determine whether these compounds affect the quantitation of digoxin concentrations using the ARCHITECT Digoxin assay. The compounds were spiked into a serum pool (containing no digoxin) and into two therapeutic levels (approximately 0.5 ng/mL and 2.0 ng/mL) of digoxin. The samples were assayed and the digoxin concentrations of the spiked samples were compared to the control serum.

The data are summarized in the following table.*

### Table: Cross-reactivity of ARCHITECT Digoxin assay

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cross-React. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>100</td>
</tr>
<tr>
<td>Digoxigenin</td>
<td>99.4</td>
</tr>
<tr>
<td>Digoxin digoxigenin</td>
<td>99.3</td>
</tr>
<tr>
<td>Digoxigenin di-digitoxoside</td>
<td>99.3</td>
</tr>
<tr>
<td>Lanatoside C</td>
<td>99.3</td>
</tr>
<tr>
<td>Proscillaridin</td>
<td>99.1</td>
</tr>
<tr>
<td>Deslanoside</td>
<td>99.1</td>
</tr>
<tr>
<td>Ouabain</td>
<td>98.9</td>
</tr>
<tr>
<td>Digitoxin</td>
<td>98.8</td>
</tr>
<tr>
<td>Progesterone</td>
<td>98.3</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>98.3</td>
</tr>
<tr>
<td>Canrenone</td>
<td>98.1</td>
</tr>
</tbody>
</table>

The mean percent recovery in this study ranged from 99.1% to 104.8%.*

The sera from patients in specific patient populations (i.e., patients with renal and/or hepatic failure, newborn infants, and pregnant women) have been reported to contain an unidentified component that gives positive results for digoxin with a number of immunoassays. This component has been called digoxin-like immunoreactive factor (DLIF) or substance (DLIS). The presence of DLIF in a sample can result in falsely elevated digoxin assay results. The amount of DLIF in these patient samples is extremely variable, but in some cases these levels have been shown to approach concentrations that are in the therapeutic range of digoxin. As with any assay employing mouse antibodies, the possibility exists for interference by HAMA in the sample, which could falsely elevate or depress results.

The manufacturer of Digoxin Immune Fab has stated that no immunosassay technique is suitable for quantitating digoxin in serum from patients on antibody fragment therapy. According to the manufacturer’s insert, DIGIBIND will interfere with digitalis immunoassay measurements. This component has been called digoxin-like immunoreactive factor (DLIF) or substance (DLIS). The presence of DLIF in a sample can result in falsely elevated digoxin assay results. The amount of DLIF in these patient samples is extremely variable, but in some cases these levels have been shown to approach concentrations that are in the therapeutic range of digoxin. As with any assay employing mouse antibodies, the possibility exists for interference by HAMA in the sample, which could falsely elevate or depress results.

### Method Comparison

The ARCHITECT Digoxin assay was designed to have a slope of 1.0 ± 0.1 and a correlation coefficient (r) of ≥ 0.95 for specimens when compared to MULTIGENT Digoxin. A study was performed using serum and plasma specimens. The data are summarized in the following table.*

### Figure: Method Comparison

![Method Comparison Graph]

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* Potentially interfering substances include the following: HAMA, Digoxin, Digoxigenin, Digitoxin, Lanatoside C, Proscillaridin, Deslanoside, Ouabain, Progesterone, Spironolactone, Canrenone, Digitoxin, Lanatoside C, Proscillaridin, Deslanoside, Ouabain, Progesterone, Spironolactone, Canrenone.

* A linear regression method with no special assumptions regarding the distribution of the sample.

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A bias analysis of ARCHITECT® Digoxin vs. MULTIGENT Digoxin was performed on the same 200 specimens in the range of 0.34 ng/mL to 3.93 ng/mL, 0.32 ng/mL to 4.46 ng/mL, respectively. The following representative data are provided to aid in understanding the difference between the two assays. The average bias exhibited by ARCHITECT® vs. MULTIGENT in this study was -10.77%. The 95% confidence interval of that average bias is -25.61% to 4.80%. Results of the study are summarized in the following graph. The vertical lines depict the typical therapeutic range of digoxin therapy.