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

Key to symbols used

- **REF**: List Number
- **IVD**: In Vitro Diagnostic Medical Device
- **2°C**: Store at 2-8°C
- **i**: Consult instructions for use
- **SN**: Serial Number
- **REAGENT LOT**: Reagent Lot
- **EC/REP**: Authorized Representative
- **LOT**: Lot Number
- **CAL**: Calibrator (A-F)
- **CONTROL**: Control Low, Medium, High (L, M, H)
- **ASSAY CD-ROM**: Assay CD-ROM
- **REACTION VESSELS**: Reaction Vessels
- **SAMPLE CUPS**: Sample Cups
- **SEPTUM**: Septum
- **REPLACEMENT CAPS**: Replacement Caps

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.
NAME
ARCHITECT CA 19-9XR

INTENDED USE
The ARCHITECT CA 19-9XR assay is a chemiluminescent microparticle immunoassay (CMA) for the quantitative determination of 1116-NS-19-9 reactive determinants in human serum or plasma on the ARCHITECT i System. The ARCHITECT CA 19-9XR assay is to be used as an aid in the management of pancreatic cancer patients in conjunction with other clinical methods.

SUMMARY AND EXPLANATION OF TEST
The ARCHITECT CA 19-9XR assay detects a tumor-associated antigen, which occurs in tissue as a monosialoganglioside and in serum as a high molecular weight, carbohydrate-rich glycoprotein known as a mucin.2-4 The ARCHITECT CA 19-9XR assay is based upon a monoclonal antibody, 1116-NS-19-9, which reacts with a carbohydrate antigenic determinant expressed on the circulating antigen.2-4

The results of published research studies6-12 indicate that the CA 19-9 assay value is frequently elevated in the serum of subjects with various gastrointestinal conditions, such as pancreatic, colorectal, gastric, and hepatic carcinomas. No data exist to support the use of CA 19-9 in screening gastrointestinal conditions, such as pancreatic, colorectal, gastric, and hepatic carcinomas.6-9,15-18 Elevated levels have also been seen in cystic fibrosis.19-22 Research studies demonstrate that CA 19-9 assay values may have utility in monitoring subjects with the above-mentioned diagnosed gastrointestinal malignancies.23-26 It has been shown that a persistent elevation in CA 19-9 assay value following treatment may be indicative of occult metastatic and/or residual disease. A persistently rising CA 19-9 assay value may be associated with progressive malignant disease and poor therapeutic response. A declining CA 19-9 assay value may be indicative of a favorable prognosis and a good response to treatment.27-33

Testing for 1116-NS-19-9 reactive determinants must not be used as a screening procedure for malignancy. 1116-NS-19-9 reactive determinants are present as a normal constituent in serum and plasma of individuals without gastrointestinal carcinomas or having certain aforementioned non-cancer related conditions.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE
The ARCHITECT CA 19-9XR assay is a two-step immunoassay for the quantitative determination of 1116-NS-19-9 reactive determinants in human serum or plasma using CMA technology with flexible assay protocols, referred to as Chemilum.

In the first step, sample and 1116-NS-19-9 coated paramagnetic microparticles are combined. 1116-NS-19-9 reactive determinants present in the sample bind to the 1116-NS-19-9 coated microparticles. After washing, 1116-NS-19-9 acridinium-labeled conjugate is added to create a reaction mixture 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 1116-NS-19-9 reactive determinants in the sample and the RLUs detected by the ARCHITECT i System optics.

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

REAGENTS
Reagent Kit, 100 Tests/500 Tests

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

ARCHITECT CA 19-9XR Reagent Kit (2K91)

- **MICROPARTICLES**
  - Bottle(s) (6.6 mL per 100 test bottle) 270.0 mL per 500 test bottle) 1116-NS-19-9 (mouse, monoclonal) coated microparticles in citrate buffer with protein (bovine) stabilizer.
  - Preservative: antimicrobial agents.

- **CONJUGATE**
  - Bottle(s) (5.9 mL per 100 test bottle) 26.3 mL per 500 test bottle) 1116-NS-19-9 (mouse, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (bovine) stabilizer.
  - Minimum concentration: 0.5 µg/mL.
  - Preservative: antimicrobial agents.

**Assay Diluent**

ARCHITECT i Multi-Assay Manual Diluent (7D82)

- **MULTI-ASSAY MANUAL DILUENT**
  - 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

**NOTE:** Bottle and volume varies based on order.

**WASH BUFFER**

- Wash Buffer containing phosphate buffered saline solution.
  - Preservative: antimicrobial agent.
WARNINGS AND PRECAUTIONS

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

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.

- The conjugate contains a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (3:1), which is a component of ProClin 300, and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases:

  - **R36** Irritating to eyes.
  - **R24** Avoid contact with skin.
  - **R26** In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
  - **R35** This material and its container must be disposed of in a safe way.
  - **S37/39** Wear suitable gloves and eye/face protection.
  - **S46** If swallowed, seek medical advice immediately and show this container or label.

- The microparticles contain a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (3:1), which is a component of ProClin 300, and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases:

  - **R43** May cause sensitization by skin contact.
  - **S24** Avoid contact with skin.
  - **S35** This material and its container must be disposed of in a safe way.
  - **S37** Wear suitable gloves.
  - **S46** If swallowed, seek medical advice immediately and show this container or label.

- This product contains 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 7.

Handling Precautions

- 1116-NS-19-9 reactive determinants are shed naturally in saliva and other body fluids. Contamination of the samples or the ARCHITECT i System disposables with saliva or aerosols (e.g., as a result of sneezing) may cause falsely elevated CA 19-9 assay values. It is recommended that all elevated values be reviewed and testing repeated as appropriate. Gloves should always be worn when handling samples, sample cups, reaction vessels, and septums. Face masks are also recommended.

- Do not re-use reagent kits beyond the expiration date.

- Do not pool reagents within a kit or between reagent lots.

- Prior to loading the ARCHITECT CA 19-9i Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend 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

- The ARCHITECT CA 19-9i 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 CA 19-9i Reagent Kit may be stored onboard 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 any reagent 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 CA 19-9i assay file must be installed on the ARCHITECT i System from the ARCHITECT i Assay CD-ROM Add-on 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.
SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Only serum (including serum collected in separator tubes) or plasma (collected in tripotassium EDTA, sodium heparin, or lithium heparin collection tubes) may be used in the ARCHITECT CA 19-9 assay. Other anticoagulants have not been validated for use with the ARCHITECT CA 19-9 assay. Follow the tube manufacturer’s processing instructions for serum and plasma collection tubes.

- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.

- 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 type is used in the ARCHITECT CA 19-9 assay.

- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.

- Performance has not been established using body fluids other than human serum or plasma.

- Specimens with obvious microbial contamination should not be used.

- Do not use grossly hemolyzed specimens.

- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.

- Serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter. Centrifuge serum and plasma specimens containing fibrin, red blood cells, or particulate matter prior to use to ensure consistency in results.

- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.

- If testing will be delayed for more than 24 hours, remove serum or plasma from the clot. Serum separator or red blood cells. Specimens may be stored for up to 7 days at 2-8°C prior to being tested. If testing will be delayed more than 7 days, specimens should be stored frozen.

- Multiple freeze-thaw cycles of specimens should be avoided. Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Sample from the middle of the tube to avoid any particulate on the top or bottom of the sample.

- Prior to shipment, it is recommended that specimens be removed from the clot, serum separator or red blood cells. When shipped, specimens must be packaged and labeled 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

- 2K91 ARCHITECT CA 19-9 Reagent Kit

Materials Required but not Provided

- ARCHITECT i System
- 3K52 ARCHITECT i ASSAY CB-ROM - WW (excluding US) Addition A
- 2K91-01 ARCHITECT CA 19-9 Controls
- 2K91-10 ARCHITECT CA 19-9 Controls
- T8D2 ARCHITECT i MULTIASSAY MANUAL DILUENT
- 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

- 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 ARCHITECT CA 19-9 Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment:

- Invert the microparticle bottle 30 times.
- Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain 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, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Carefully snap the septum onto the top of the bottle.

- 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.

- Load the ARCHITECT CA 19-9 Reagent Kit on the ARCHITECT i System. Verify that all necessary assay reagents are present. Ensure that septums are present on all reagent bottles.

- The minimum sample 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 that adequate sample cup volume is present before running the test.

- Priority: 80 µL for the first ARCHITECT CA 19-9 test plus 30 µL for each additional test from the same sample cup.

- < 3 hours on board: 150 µL for the first ARCHITECT CA 19-9 test plus 30 µL for each additional ARCHITECT CA 19-9 test from the same sample cup.

- > 3 hours on board: additional sample volume is required. Refer to the Architect System Operations Manual, Section 5 for information on sample evaporation and volumes.

- If using primary or aliquot tubes, use the sample gauge to ensure that sufficient patient specimen is present.

- Prepare calibrators and controls.

- ARCHITECT CA 19-9 Controls and Calibrators should be mixed by gentle inversion before use.

- To obtain the recommended volume requirements for the ARCHITECT CA 19-9 Controls and Calibrators, hold the bottles vertically and dispense 4 drops of each calibrator or 4 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. The ARCHITECT i-System performs the following functions:
  • Moves the sample to the aspiration point
  • Loads a reaction vessel (RV) into the process path
  • Aspirates and transfers sample into the RV
  • Advances the RV one position and transfers microparticles into the RV
  • Mixes, incubates and washes the reaction mixture
  • Adds conjugate to the RV
  • Mixes, incubates and washes the reaction mixture
  • Adds Pre-Triger and Trigger Solutions
  • Measures chemiluminescent emission to determine the quantity of 1116-NS-19-9 reactive determinants in the sample
  • Aspirates contents of RV to liquid waste and unloads RV to solid waste
  • Calculates the result

For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with an ARCHITECT CA 19-9 XR assay value exceeding 1200 U/mL are flagged with the code “>1200.00” and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

If using the Automated Dilution Protocol, the system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the sample before dilution and reports the result.

Manual dilutions should be performed as follows:
  • The suggested dilution for the ARCHITECT CA 19-9 XR assay is 1:10. An additional 1:10 dilution may be made if needed.
  • For a 1:10 dilution, add 50 µL of the patient specimen to 450 µL of ARCHITECT i Multi-Assay Manual Diluent (7D82).
  • The operator must enter the dilution factor in the Patient or Control order screen. All assays selected for that order will be diluted. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The dilution should be performed so that the diluted result reads greater than 30 U/mL.
  • For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

To perform an ARCHITECT CA 19-9 XR calibration, test calibrators A, B, C, D, E, and F in duplicate. A single sample of each CA 19-9 control 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.

Calibrator Range: 0 - 1200 U/mL

Once an ARCHITECT CA 19-9 XR 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 CA 19-9 XR assay is that a single sample of each control level 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 your laboratory-specific procedures.

The ARCHITECT CA 19-9 XR values must be within the acceptable ranges specified in the control package insert. If a control is out of the 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 CA 19-9 XR assay belongs to method group 1.

RESULTS

Calculation

• The ARCHITECT CA 19-9 XR assay uses 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

• The ARCHITECT CA 19-9 XR assay must be used in conjunction with information available from clinical evaluation and other diagnostic procedures.

• If the ARCHITECT CA 19-9 XR assay results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

• Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoaassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed.

• 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 that employ mouse monoclonal antibodies. ARCHITECT CA 19-9 XR reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.

• Patients with confirmed carcinoma may have pretreatment CA 19-9 assay values in the same range as healthy individuals. Elevations in circulating 1116-NS-19-9 reactive determinants may be observed in patients with metastases and in nonmalignant conditions such as hepatitis, cirrhosis, pancreatitis, and other gastrointestinal disease. Elevated levels have also been seen in cystic fibrosis. For these reasons, a CA 19-9 assay value, regardless of level, should not be interpreted as absolute evidence for the presence or absence of malignant disease. The ARCHITECT CA 19-9 XR assay must not be used as a cancer screening test.

• Patients with the Le A- phenotype may not express the 1116-NS-19-9 reactive determinant.

• Representative performance data are given in the EXPECTED VALUES and SPECIFIC PERFORMANCE CHARACTERISTICS sections. Results obtained in individual laboratories may vary.
EXPECTED VALUES

APPELLANTLY HEALTHY SUBJECTS

A study was performed with three hundred sixty (360) serum specimens from apparently healthy individuals. The distribution of ARCHITECT CA 19-9 values from these specimens is shown in the table below.*

<table>
<thead>
<tr>
<th>Distribution of ARCHITECT CA 19-9 Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent (%)</td>
</tr>
<tr>
<td>Number of Subjects</td>
</tr>
<tr>
<td>Subjects (U/mL)</td>
</tr>
<tr>
<td>Apparently Healthy Subjects</td>
</tr>
</tbody>
</table>

In this study, 94.4% of the specimens from apparently healthy subjects (n=360) had values of 37 U/mL or less.

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

NONMALIGNANT DISEASE

A study was performed with four hundred forty one (441) samples from patients with nonmalignant disease to determine the distribution of serum ARCHITECT CA 19-9 values. The distribution of values determined in this study is shown in the table below.*

<table>
<thead>
<tr>
<th>Distribution of ARCHITECT CA 19-9 Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent (%)</td>
</tr>
<tr>
<td>Number of Subjects</td>
</tr>
<tr>
<td>Subjects (U/mL)</td>
</tr>
<tr>
<td>Rectal Polyps</td>
</tr>
<tr>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Gallbladder</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Pulmonary</td>
</tr>
<tr>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Hepatitis</td>
</tr>
<tr>
<td>Renal</td>
</tr>
<tr>
<td>Other Gastrointestinal</td>
</tr>
</tbody>
</table>

The ARCHITECT CA 19-9 assay is used in conjunction with other clinical methods in the management of cancer patients.

It is recommended that each laboratory establish its own reference value for the population of interest.

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

Monitoring of Disease State in Patients Diagnosed with Pancreatic Cancer

Changes observed in serial CA 19-9 assay values when monitoring pancreatic cancer patients must be evaluated in conjunction with other clinical methods.

The effectiveness of the ARCHITECT CA 19-9 assay as an aid in monitoring of disease state in pancreatic cancer patients was determined by assessing changes in levels of 1116-NS-19-9 reactive determinants in serial serum samples from 74 patients compared to changes in disease state. A study involving a total of 261 observations was performed with an average number of 3.5 observations per patient. In this study a significant change in levels of 1116-NS-19-9 reactive determinants was defined as an increase or decrease in assay value of at least a 14.0% change in levels of 1116-NS-19-9 reactive determinants was defined as at least a 14% increase in assay value and disease progression was found to be 48% (16/33). Negative concordance between serial samples with less than a 14.0% increase in assay value and no disease progression was found to be 69% (15/22). The following table presents the data in a 2 x 2 classification scheme.*

<table>
<thead>
<tr>
<th>Determinants</th>
<th>Progression</th>
<th>No Progression</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;14.0%</td>
<td>17</td>
<td>98</td>
<td>115</td>
</tr>
<tr>
<td>≥14.0%</td>
<td>15</td>
<td>16</td>
<td>31</td>
</tr>
</tbody>
</table>

The following table provides the per patient distribution.*. Positive concordance between serial samples with at least a 14.0% increase in assay value and disease progression was found to be 68% (15/22). Negative concordance between serial samples with less than a 14.0% increase in assay value and no disease progression was found to be 69% (36/52). The overall concordance was found to be 69% (51/74).

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

Below are examples of serial monitoring profiles for two patients with the disease state, ARCHITECT CA 19-9 assay values, and the CA 19-9 RIA values.* The disease states are:

- Progression from one collection to the next collection (Progression).
- No Change in disease state (Stable).
- Reduction in the signs and symptoms of the disease from one collection to the next (Responding).

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

Precision
The ARCHITECT CA 19-9XR assay is designed to have an assay precision of ≤10% total CV.

A study was performed as described per the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A2. Six samples were tested consisting of two panels of pooled serum (panels 1 and 2), one panel of serum to which 1116-NS-19-9 reactive determinants were added (panel 3), and the three ARCHITECT CA 19-9XR Controls. Testing was performed using two lots of reagents, in replicates of two at two separate times per day for 20 days on two separate instruments. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized below.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>Reagent Lot</th>
<th>Instrument n</th>
<th>Mean Conc. (U/mL)</th>
<th>Within Run SD</th>
<th>Total %CV</th>
<th>Total SD</th>
<th>Total %CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panel 1</td>
<td>1</td>
<td>80</td>
<td>56.52</td>
<td>1.69</td>
<td>3.0</td>
<td>2.19</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>80</td>
<td>51.20</td>
<td>1.80</td>
<td>3.5</td>
<td>2.10</td>
<td>4.1</td>
</tr>
<tr>
<td>Panel 2</td>
<td>1</td>
<td>80</td>
<td>311.49</td>
<td>7.22</td>
<td>2.3</td>
<td>10.72</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>80</td>
<td>288.82</td>
<td>9.14</td>
<td>3.2</td>
<td>11.23</td>
<td>3.9</td>
</tr>
<tr>
<td>Panel 3</td>
<td>1</td>
<td>80</td>
<td>744.81</td>
<td>27.82</td>
<td>3.7</td>
<td>36.85</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>80</td>
<td>728.82</td>
<td>42.53</td>
<td>5.8</td>
<td>47.66</td>
<td>6.5</td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td>80</td>
<td>45.03</td>
<td>2.59</td>
<td>5.8</td>
<td>2.98</td>
<td>6.6</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>42.33</td>
<td>2.94</td>
<td>6.9</td>
<td>3.60</td>
<td>8.5</td>
</tr>
<tr>
<td>Medium</td>
<td>1</td>
<td>80</td>
<td>157.66</td>
<td>5.99</td>
<td>3.8</td>
<td>8.52</td>
<td>5.4</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>146.93</td>
<td>6.26</td>
<td>4.3</td>
<td>8.14</td>
<td>5.5</td>
</tr>
<tr>
<td>High</td>
<td>1</td>
<td>80</td>
<td>781.68</td>
<td>44.76</td>
<td>5.7</td>
<td>49.87</td>
<td>6.4</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>781.42</td>
<td>62.10</td>
<td>8.0</td>
<td>65.26</td>
<td>8.4</td>
</tr>
</tbody>
</table>

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

Recovery
The ARCHITECT CA 19-9XR assay is designed to have a mean recovery of 100 ± 15% when 1116-NS-19-9 reactive determinants are added to serum samples.

A study was performed for the ARCHITECT CA 19-9XR assay based on guidance from Tietz Textbook of Clinical Chemistry. Known concentrations of 1116-NS-19-9 reactive determinants were added to human serum samples. The concentration of 1116-NS-19-9 reactive determinants was determined using the ARCHITECT CA 19-9XR assay, and the resulting percent recovery was calculated. Representative data from this study are summarized in the table below.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>Endogenous Assay Value (U/mL)</th>
<th>1116-NS-19-9 Reactive Determinants Added (U/mL)</th>
<th>Observed ARCHITECT CA 19-9XR Assay Value (U/mL)</th>
<th>% Recovery**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46.50</td>
<td>124.21</td>
<td>152.42</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>629.91</td>
<td>645.00</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>28.96</td>
<td>124.21</td>
<td>146.73</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td>629.91</td>
<td>598.93</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>38.42</td>
<td>124.21</td>
<td>175.18</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td></td>
<td>629.91</td>
<td>652.12</td>
<td>98</td>
</tr>
</tbody>
</table>

Mean recovery across two separate spiked concentrations shown above = 96%

% Recovery = \( \frac{\text{Observed (U/mL)}}{\text{Endogenous Level (U/mL)} + 1116-NS-19-9 \text{ Reactive Determinants Added (U/mL)}} \times 100 \)

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

Dilution Linearity
The ARCHITECT CA 19-9XR assay is designed to have a mean recovery of 100 ± 15% of the expected result for diluted specimens.

A study was performed for the ARCHITECT CA 19-9XR assay modeled after the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP6-P2.4 Samples with known elevated 1116-NS-19-9 reactive determinant concentrations were diluted with ARCHITECT i Multi-Assay Manual Diluent. The 1116-NS-19-9 reactive determinants concentration was determined for each dilution and the percent recovery was calculated. Representative data from this study are summarized below.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>Final Dilution Factor</th>
<th>Expected Value (U/mL)</th>
<th>Value Obtained (U/mL)</th>
<th>% Recovery**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 undiluted</td>
<td>1024.55</td>
<td>1024.55</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1.2</td>
<td>512.27</td>
<td>472.46</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>256.14</td>
<td>264.26</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>204.91</td>
<td>208.57</td>
<td>102</td>
</tr>
<tr>
<td></td>
<td>1.10</td>
<td>102.45</td>
<td>108.94</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>1.20</td>
<td>51.23</td>
<td>54.33</td>
<td>106</td>
</tr>
<tr>
<td>2</td>
<td>1 undiluted</td>
<td>1150.50</td>
<td>1150.50</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1.2</td>
<td>575.25</td>
<td>551.62</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>287.63</td>
<td>291.06</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>230.10</td>
<td>253.65</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td>1.10</td>
<td>115.05</td>
<td>125.97</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>1.20</td>
<td>57.53</td>
<td>62.57</td>
<td>109</td>
</tr>
<tr>
<td>3</td>
<td>1 undiluted</td>
<td>1028.25</td>
<td>1028.25</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1.2</td>
<td>514.12</td>
<td>492.39</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>257.06</td>
<td>250.24</td>
<td>113</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>205.65</td>
<td>204.03</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>1.10</td>
<td>102.82</td>
<td>120.76</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>1.20</td>
<td>51.41</td>
<td>57.25</td>
<td>111</td>
</tr>
</tbody>
</table>

Mean recovery across the three diluted samples shown above = 105%

% Recovery = \( \frac{\text{Value Obtained (U/mL)}}{\text{Dilution Factor} \times \text{Undiluted Expected Value (U/mL)}} \)

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

Analytical Sensitivity
The analytical sensitivity of the ARCHITECT CA 19-9XR assay was calculated to be better than 2.00 U/mL (n = 18 runs, in replicates of 10). Analytical sensitivity is defined as the concentration at two standard deviations from the ARCHITECT CA 19-9XR Calibrator A (0 U/mL), and represents the lowest measurable concentration of 1116-NS-19-9 reactive determinants that can be distinguished from zero.

Mean recovery across two separate spiked concentrations shown above = 96%

% Recovery = \( \frac{\text{Observed (U/mL)}}{\text{Endogenous Level (U/mL)} + 1116-NS-19-9 \text{ Reactive Determinants Added (U/mL)}} \times 100 \)

* Representative data; results in individual laboratories may vary from these data.
A study based on guidance from the NCCLS Protocol EP7-A45 was performed for the ARCHITECT CA 19-9 assay. Specimens with 1116-NS-19-9 reactive determinants between 49.6 and 509.4 U/mL were supplemented with the following potentially interfering substances and chemotherapeutic agents.

**POTENTIALLY INTERFERING SUBSTANCES**

The average recovery observed during the study ranged from 91% to 102%.*

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>22 mg/dL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>600 mg/dL</td>
</tr>
<tr>
<td>Total Protein</td>
<td>10 g/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>5100 mg/dL</td>
</tr>
</tbody>
</table>

**CHEMOTHERAPEUTIC AGENTS**

The average recovery observed during the study ranged from 95% to 104%.*

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>0.390 mg/mL</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>0.057 mg/mL</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>0.375 mg/mL</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>30 µg/mL</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>40 µg/mL</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>0.382 mg/mL</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>0.114 mg/mL</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0.909 mg/mL</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>0.067 mg/mL</td>
</tr>
<tr>
<td>Streptozotin</td>
<td>0.28 mg/mL</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>2.28 µg/dL</td>
</tr>
</tbody>
</table>

**EVALUATION OF POTENTIALLY INTERFERING CLINICAL CONDITIONS**

The ARCHITECT CA 19-9® assay is designed to have a mean recovery of 100 ± 12% in the presence of HAMA and rheumatoid factor (RF).

The ARCHITECT CA 19-9® assay was evaluated using specimens with HAMA and RF to further assess the clinical specificity. Five specimens positive for HAMA and five specimens positive for RF were evaluated for % recovery with 1116-NS-19-9 reactive determinants spiked into each specimen at 35 and 250 U/mL. Mean percent recovery results are summarized in the following table.*

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>Number of Specimens</th>
<th>Mean % Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMA</td>
<td>10</td>
<td>93</td>
</tr>
<tr>
<td>RF</td>
<td>10</td>
<td>93</td>
</tr>
</tbody>
</table>

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

**Carryover**

No significant carryover (less than 2.00 U/mL in CA19-9mol Calibrator A*) was observed for the ARCHITECT CA 19-9® assay when a sample containing up to 320,000 U/mL of 1116-NS-19-9 reactive determinants was assayed.

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

**High Dose Hook**

No high dose hook effect was observed for the ARCHITECT CA 19-9® assay when samples containing up to 1,750,000 U/mL* of 1116-NS-19-9 reactive determinants were assayed. High dose hook is a phenomenon whereby very high level specimens may falsely read within the dynamic range of the assay.

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

**BIBLIOGRAPHY**


