ARCHITECT
CA 19-9XR

REF 2K91-24
REF 2K91-32
REF 2K91-39

en
CA 19-9XR
2K91
613-031 11/16/R03
B2K9Y0

Read Highlighted Changes: Revised November 2016.

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.

WARNING: The Abbott ARCHITECT CA 19-9XR CMIA assay utilizes an antibody/antigen system based on the 1116-NS-19-9 antibody. The unique reagent formulation employed in the ARCHITECT CA 19-9XR assay may return elevated concentrations when compared to other methods for samples expressing high levels of 1116-NS-19-9 reactive determinants.[1, 2] Additionally, there is no internationally recognized standard for CA 19-9, which can contribute to differences between assay methods. The ARCHITECT CA 19-9XR assay is standardized to a reference standard prepared by Fujirebio Diagnostics, Inc. Performance characteristics of the Abbott ARCHITECT CA 19-9XR assay are NOT transferable to other diagnostic kits.

The concentration of 1116-NS-19-9 reactive determinants obtained with different assay methods cannot be used interchangeably due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the CA 19-9 assay used. If, in the course of monitoring a patient, the assay method used for determining serial 1116-NS-19-9 reactive determinant levels is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

WARNING: 1116-NS-19-9 reactive determinants are shed naturally in saliva and other body fluids.[3] Contamination of the samples or the ARCHITECT iSystem 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.

NAME

ARCHITECT CA 19-9XR

INTENDED USE

The ARCHITECT CA 19-9XR assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of 1116-NS-19-9 reactive determinants in human serum or plasma on the ARCHITECT iSystem. 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 THE 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.[4-7]

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.[4-6]

The results of published research studies[8-14] 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 for malignancies.[15, 16] The role of CA 19-9 is to be used as an adjunct with other diagnostic information in the management of patients with pancreatic cancer.[15] Increased serum CA 19-9 assay values have also been observed in patients with metastases and in nonmalignant conditions such as hepatitis, cirrhosis, pancreatitis, and other gastrointestinal disease.[8-11, 17-20] Elevated levels have also been seen in cystic fibrosis.[21-24] Research studies demonstrate that CA 19-9 assay values may have utility in monitoring subjects with the above-mentioned diagnosed gastrointestinal malignancies.[25-28] 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.[29-35]

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 CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and 1116-NS-19-9 coated paramagnetic microparticles are combined. The 1116-NS-19-9 reactive determinants present in the sample bind to the 1116-NS-19-9 coated microparticles.
2. After washing, 1116-NS-19-9 acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of 1116-NS-19-9 reactive determinants in the sample and the RLUs detected by the ARCHITECT iSystem optics.

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

REAGENTS

Kit Contents

ARCHITECT CA 19-9XR 2K91

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

REF	2K91-32	2K91-24	2K91-39
Σ	100	400	500
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL

MICROPARTICLES 1116-NS-19-9 (mouse, monoclonal) coated microparticles in citrate buffer with protein (bovine) stabilizer. Minimum concentration: 0.09% solids. Preservatives: sodium azide and ProClin 300.

CONJUGATE 1116-NS-19-9 (mouse, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (bovine) stabilizer. Minimum concentration: 0.5 µg/mL. Preservatives: sodium azide and ProClin 300.

Other Reagents

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

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

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

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

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[36-39]

The following warnings and precautions apply to: MICROPARTICLES

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

The following warnings and precautions apply to: CONJUGATE

DANGER	Contains polyethylene glycol octylphenyl ether, methylisothiazolones and sodium azide.
H317	May cause an allergic skin reaction.
H318	Causes serious eye damage.
H412	Harmful to aquatic life with long lasting effects.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P280	Wear protective gloves / protective clothing / eye protection.
P272	Contaminated work clothing should not be allowed out of the workplace.
P273	Avoid release to the environment.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310	Immediately call a POISON CENTER or doctor / physician.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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

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

Reagent Handling

- **1116-NS-19-9 reactive determinants are shed naturally in saliva and other body fluids.[3] Contamination of the samples or the ARCHITECT iSystem 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 use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**

- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
- Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

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

Reagent Storage

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

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

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8˚C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright.

If 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 19-9XR assay file must be installed on the ARCHITECT iSystem prior to performing the assay.

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

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

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

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Serum	Serum Serum separator tubes
Plasma	Tripotassium EDTA Sodium Heparin Lithium Heparin

- Other specimen collection tube types have not been tested with this assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.
- 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.

Specimen Conditions

- Do not use specimens with the following conditions:
  - grossly hemolyzed
  - obvious microbial contamination
- 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.
- Performance has not been established using body fluids other than human serum or plasma.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

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

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8˚C	≤ 7 days
	-20˚C or colder	>7 days

- If testing will be delayed 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, serum or plasma should be stored frozen at -20˚C or colder.
- Avoid multiple freeze/thaw cycles.

Specimen Shipping

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

PROCEDURE

Materials Provided

2K91 ARCHITECT CA 19-9XR Reagent Kit

Materials Required but not Provided

- ARCHITECT CA 19-9XR Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 2K91 ARCHITECT CA 19-9XR Calibrators
- 2K91 ARCHITECT CA 19-9XR Controls
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

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

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

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

    Sample volume for first test: 80 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - > 3 hours on board: Additional sample volume required
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT CA 19-9XR Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 4 drops

    for each control: 4 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with an ARCHITECT CA 19-9XR 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.

Automated Dilution Protocol

The system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Manual Dilution Procedure

Suggested dilution: 1:10

An additional 1:10 dilution may be made if needed.

1. Add 50 µL of the patient specimen to 450 µL of ARCHITECT Multi-Assay Manual Diluent (7D82).
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The 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

- Test Calibrators A-F in duplicate. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0 - 1200 U/mL.
- Once an ARCHITECT CA 19-9XR calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT CA 19-9XR assay is that a single sample of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

The ARCHITECT CA 19-9XR 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 19-9XR assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT CA 19-9XR assay utilizes a Linear Regression 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

- The ARCHITECT CA 19-9XR assay value must be used in conjunction with information available from clinical evaluation and other diagnostic procedures.
- If the ARCHITECT CA 19-9XR results are inconsistent with clinical evidence, additional testing is recommended.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed.[40]
- 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 19-9XR reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.[41, 42]
- 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.[21] 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 19-9XR assay must not be used as a cancer screening test.**
- Patients with the Le^{a-b-} phenotype may not express the 1116-NS-19-9 reactive determinant.[43]
- Representative performance data are given in the **EXPECTED VALUES and SPECIFIC PERFORMANCE CHARACTERISTICS** sections. Results obtained in individual laboratories may vary.

EXPECTED VALUES

APPARENTLY HEALTHY SUBJECTS

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

Distribution of ARCHITECT CA 19-9XR Values

		Percent (%)				
	Number of Subjects	0-37.0 (U/mL)	37.1-100 (U/mL)	100.1-500 (U/mL)	500.1-1200 (U/mL)	>1200 (U/mL)
Apparently Healthy Subjects	360	94.4	5.6	0.0	0.0	0.0

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 19-9XR assay values. The distribution of values determined in this study is shown in the table below.*

Distribution of ARCHITECT CA 19-9XR Values

		Percent (%)				
Nonmalignant Disease	Number of Subjects	0-37.0 (U/mL)	37.1-100 (U/mL)	100.1-500 (U/mL)	500.1-1200 (U/mL)	>1200 (U/mL)
Rectal Polyps	33	97.0	3.0	0.0	0.0	0.0
Pancreatitis	3	100.0	0.0	0.0	0.0	0.0
Gallbladder	21	95.2	0.0	0.0	0.0	4.8
Diabetes	38	94.7	5.3	0.0	0.0	0.0
Pulmonary	40	100.0	0.0	0.0	0.0	0.0
Cirrhosis	153	92.8	4.6	0.7	0.7	1.3
Hepatitis	68	92.6	7.4	0.0	0.0	0.0
Renal	34	91.2	8.8	0.0	0.0	0.0
Other Gastrointestinal	51	96.1	3.9	0.0	0.0	0.0

The ARCHITECT CA 19-9XR 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 19-9XR 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 at least a 14.0% increase in assay value (i.e., 2.5 times greater than the average of the assay's observed total %CV [5.6%]). A 14.0% change represents the minimum magnitude change between two serial ARCHITECT CA 19-9XR measurements that could not be attributed to assay variation or noise. Positive concordance between serial samples with at least a 14.0% 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 64% (98/154). The overall concordance was found to be 61% (114/187). The following table presents the data in a 2 x 2 classification scheme*.

Change in Disease State per Sequential Pair

Change in the Level of 1116-NS-19-9 Reactive Determinants	Progression	No Progression	Total
≥14.0%	16	56	72
<14.0%	17	98	115
Total	33	154	187

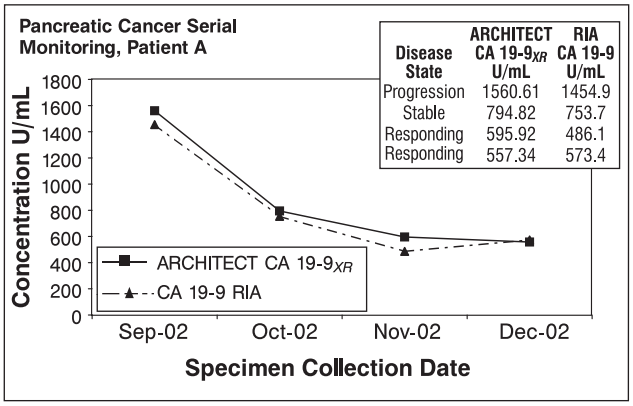
The following table provides the per patient distribution*. Positive concordance between serial samples with at least a 14.0% increase in assay value and disease progression was found to be 68% (15/22). Negative concordance between serial samples with less than a 14.0% increase in assay value and no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

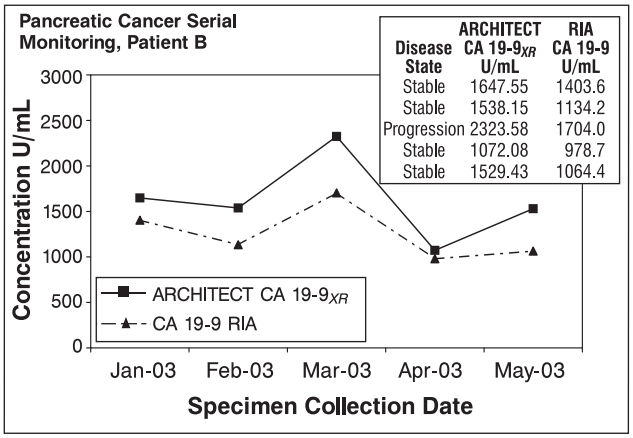
Change in Disease State per Patient			
Change in the Level of 1116-NS-19-9 Reactive Determinants	Progression	No Progression	Total
≥14.0%	15	16	31
<14.0%	7	36	43
Total	22	52	74

* 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 19-9XR 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.[44] 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.*

Sample	Reagent Lot	Instrument	n	Mean Conc. (U/mL)	Within Run SD	Within Run %CV	Total SD	Total %CV
Panel 1	1	1	80	56.52	1.69	3.0	2.19	3.9
	2	2	80	51.20	1.80	3.5	2.10	4.1
Panel 2	1	1	80	311.49	7.22	2.3	10.72	3.4
	2	2	80	288.82	9.14	3.2	11.23	3.9
Panel 3	1	1	80	744.81	27.82	3.7	36.85	5.0
	2	2	80	728.82	42.53	5.8	47.66	6.5
Low Control	1	1	80	45.03	2.59	5.8	2.98	6.6
	2	2	80	42.33	2.94	6.9	3.60	8.5
Medium Control	1	1	80	157.66	5.99	3.8	8.52	5.4
	2	2	80	146.93	6.26	4.3	8.14	5.5
High Control	1	1	80	781.68	44.76	5.7	49.87	6.4
	2	2	80	781.42	62.10	8.0	65.28	8.4

* 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.[45] 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.*

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

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

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

* 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.[46] Samples with known elevated 1116-NS-19-9 reactive determinant concentrations were diluted with ARCHITECT 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.*

Sample	Final Dilution Factor	Expected Value (U/mL)	Value Obtained (U/mL)	% Recovery**
1	Undiluted	1024.55	1024.55	-
	1:2	512.27	472.46	92
	1:4	256.14	264.26	103
	1:5	204.91	208.57	102
	1:10	102.45	108.94	106
	1:20	51.23	54.33	106
2	Undiluted	1150.50	1150.50	-
	1:2	575.25	551.62	96
	1:4	287.63	291.06	101
	1:5	230.10	253.65	110
	1:10	115.05	125.97	109
	1:20	57.53	62.57	109
3	Undiluted	1028.25	1028.25	-
	1:2	514.12	492.39	96
	1:4	257.06	290.24	113
	1:5	205.65	204.03	99
	1:10	102.82	120.76	117
	1:20	51.41	57.25	111

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

$$** \% \text{ Recovery} = \frac{\text{Values Obtained x Dilution Factor}}{\text{Undiluted Expected Value}} \text{ x } 100$$

* 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.

Interference

The ARCHITECT CA 19-9XR assay is designed to have a mean recovery of 100 ± 12% in the presence of the chemotherapeutic agents listed below and elevated levels of bilirubin, hemoglobin, triglycerides, and total protein at the levels indicated.

A study based on guidance from the NCCLS Protocol EP7-A[47] was performed for the ARCHITECT CA 19-9XR assay. Specimens with 1116-NS-19-9 reactive determinant levels 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%.*

Substance	Concentration
Bilirubin	22 mg/dL
Hemoglobin	600 mg/dL
Total Protein	10 g/dL
Triglycerides	5100 mg/dL

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

CHEMOTHERAPEUTIC AGENTS

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

Substance	Concentration
5-Fluorouracil	0.390 mg/mL
Cisplatin	0.057 mg/mL
Cyclophosphamide	0.375 mg/mL
Cytarabine	30 µg/mL
Doxorubicin	40 µg/mL
Gemcitabine	0.382 mg/mL
Leucovorin	0.114 mg/mL
Methotrexate	0.909 mg/mL
Paclitaxel	0.067 mg/mL
Streptozotocin	0.28 mg/mL
Tamoxifen	2.28 µg/dL

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

EVALUATION OF POTENTIALLY INTERFERING CLINICAL CONDITIONS

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

The ARCHITECT CA 19-9XR 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.*

Clinical Condition	Number of Specimens	Mean % Recovery
HAMA	10	93
RF	10	93

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

Carryover

No significant carryover (less than 2.00 U/mL in CA19-9XR Calibrator A*) was observed for the ARCHITECT CA 19-9XR 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 19-9XR 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.

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
ECO HAZARD	Ecological hazard
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF USA	Product of USA
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer


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