Read Highlighted Changes: Revised August 2018.

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

WARNING: CA 125 assay values 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 125 assay used. If, in the course of monitoring a patient, the assay method used for determining serial CA 125 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.

NAME

ARCHITECT CA 125 II

INTENDED USE

The ARCHITECT CA 125 II assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of OC 125 defined antigen in human serum and plasma on the ARCHITECT iSystem.

The ARCHITECT CA 125 II assay is to be used as an aid in monitoring response to therapy for patients with epithelial ovarian cancer. Serial testing for patient CA 125 II assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

SUMMARY AND EXPLANATION OF THE TEST

CA 125 II assay values are defined by using the OC 125 monoclonal antibody. OC 125 was generated through the hybridization of mouse myeloma cells to spleen cells from a mouse immunized with a human serous cystadenocarcinoma cell line called OVCA 433.[1] ARCHITECT CA 125 II is a second-generation assay for the detection of OC 125 defined antigen. The assay utilizes the OC 125 monoclonal antibody, as the capture antibody coated onto paramagnetic microparticles that bind molecules containing OC 125 defined antigen. These defined antigens are quantified using acridinium-labeled M11 antibody. The OC 125 monoclonal antibody is reactive with repeating OC 125 defined antigen expressed by a high percentage of nonmucinous ovarian carcinomas (serous, endometrioid, clear cell, and undifferentiated histologies) and epithelial ovarian carcinoma cell lines.[1, 2] OC 125 defined antigens were originally detected in normal peritoneal, pleural and pericardial tissues of both fetus and adult. In the fetus, OC 125 defined antigens have been localized in amniotic and umbilical epithelial and Müllerian epithelial tissues. In the adult, localization has been identified in endocervical and endometrial tissues and ovarian inclusion cysts and papillary excrescences. However, OC 125 defined antigens were not detected in fetal ovarian tissue or other normal adult ovarian tissues or benign mucinous ovarian tumors.[3] In serum, the OC 125 defined antigens are associated with high molecular weight glycoproteins heterogeneous in size and charge. The structure of the CA 125 molecule, including closely situated repeating epitopes for OC 125 and M11 antibodies has been proposed.[4]

Serum CA 125 II assay values are useful for monitoring the course of disease in patients with invasive epithelial ovarian cancer.[5] In a review of nine published studies, the overall correlation reported between CA 125 serum levels and the course of the disease was 87%.[6] Persistently rising CA 125 assay values may be associated with malignant disease and poor response to therapy, whereas decreasing CA 125 assay values may indicate a favorable response to therapy.[6-14]

A second-look, exploratory laparotomy may have been performed previously to assess response to therapy. The benefit has recently come into question because of high morbidity and low sensitivity in detecting residual or recurrent carcinoma.[15] In women with primary epithelial ovarian carcinoma who had undergone first-line therapy and were candidates for diagnostic second-look procedures, a CA 125 assay value greater than or equal to 35 U/mL was found to be indicative of the presence of residual tumor.[6, 9, 11, 13] However, a CA 125 assay value below 35 U/mL does not indicate the absence of residual ovarian cancer because patients with histopathologic evidence of ovarian carcinoma may have CA 125 assay values within the range of normal individuals.[7, 8]

Elevations of CA 125 assay values have been reported in approximately 1-2% of healthy individuals,[6, 7] and in individuals with nonmalignant conditions such as cirrhosis,[16, 17] hepatitis,[17, 18] endometriosis,[19-24] first trimester pregnancy,[25-27] ovarian cysts,[3, 28] and pelvic inflammatory disease.[10, 25] Elevations of CA 125 assay values during the menstrual cycle have also been reported.[23, 29] Non-ovarian malignancies in which CA 125 assay values have been reported include endocervical,[30] liver,[18] pancreatic,[18, 31] lung,[18] colon,[18, 31] stomach,[18, 31] biliary tract,[18, 31] uterine,[17] fallopian tube,[30] breast,[18] and endometrial carcinomas.[30, 32] The CA 125 assay is not recommended as a screening procedure to detect cancer in the general population; however, the use of CA 125 assay values as an aid in the management of ovarian cancer patients has been reported.[7-14]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT CA 125 II assay is a two-step immunoassay for the quantitative determination of OC 125 defined antigen in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and OC 125 coated paramagnetic microparticles are combined. The OC 125 defined antigen present in the sample binds to the OC 125 coated microparticles.
2. After washing, M11 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 OC 125 defined antigen 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 125 II 2K45

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

REF	2K45-29	2K45-24	2K45-39
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 anti-CA 125 (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers. Minimum concentration: 0.09% solids. Preservatives: Sodium Azide and ProClin 300.

CONJUGATE anti-CA 125 (mouse, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (bovine) stabilizers. Minimum concentration: 0.075 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.[33-36]

The following warnings and precautions apply to: MICROPARTICLES and CONJUGATE	
	
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.

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

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

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - **To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.**
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

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

Reagent Storage

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

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

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If 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 125 II 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 sample 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.
- 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:
  - heat-inactivated
  - grossly hemolyzed
  - obvious microbial contamination
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.
- 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 and 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 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

2K45 ARCHITECT CA 125 II Reagent Kit

Materials Required but not Provided

- ARCHITECT CA 125 II Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 2K45 ARCHITECT CA 125 II Calibrators
- 2K45 ARCHITECT CA 125 II 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: 75 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - > 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 sufficient patient specimen is present.
- Prepare ARCHITECT CA 125 II 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:

    To obtain the recommended 150 µL volume requirement for the ARCHITECT CA 125 II Calibrators dispense 4 drops.

    To obtain the recommended 150 µL volume requirement for the ARCHITECT CA 125 II Controls dispense 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 CA 125 II value exceeding 1000 U/mL are flagged with the code "> 1000.0 U/mL" and may be diluted with 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.
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 20 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 - 1000 U/mL.
- Once an ARCHITECT CA 125 II 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 125 II 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.

Ensure that assay control values are within the concentration ranges specified in the package insert.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT CA 125 II assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT CA 125 II assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Measurement Range (Reportable Range)

The measurement range for the ARCHITECT CA 125 II assay is 1.0 U/mL to 1000 U/mL.

LIMITATIONS OF THE PROCEDURE

- Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.
- If the ARCHITECT CA 125 II 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. Additional information may be required for diagnosis.[37]
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT CA 125 II that employ mouse monoclonal antibodies. Additional clinical or diagnostic information may be required to determine patient status.[38-40]
- Patients with confirmed ovarian carcinoma may have pretreatment CA 125 assay values in the same range as healthy individuals. Elevations in circulating OC 125 defined antigen may be observed in patients with nonmalignant disease. For these reasons, a CA 125 assay value, regardless of level, should not be interpreted as absolute evidence for the presence or absence of malignant disease. The CA 125 assay value should be used in conjunction with information available from clinical evaluation and other diagnostic procedures. **The ARCHITECT CA 125 II assay should not be used as a cancer screening test**.
- Representative performance data are given in the **EXPECTED VALUES** and **SPECIFIC PERFORMANCE CHARACTERISTICS** sections. Results obtained in individual laboratories may vary.

EXPECTED VALUES

The distribution of CA 125 II assay values determined in 811 specimens is shown in the table below:

Distribution of ARCHITECT CA 125 II Assay Values

		Percent (%)			
	Number of Subjects	0-35 U/mL	35.1-65 U/mL	65.1-100 U/mL	>100 U/mL
APPARENTLY HEALTHY					
Females (Premenopausal)	99	89.9	6.1	4.0	0.0
Females (Postmenopausal)	97	99.0	1.0	0.0	0.0
MALIGNANT CONDITIONS					
Ovarian Cancer	166	49.9	14.3	4.8	32.8
Breast Cancer	50	80.0	20.0	0.0	0.0
Colorectal Cancer	50	84.0	4.0	10.0	2.0
Endometrial Cancer	25	96.0	4.0	0.0	0.0
Lung Cancer	50	60.0	18.0	10.0	12.0
NONMALIGNANT CONDITIONS					
Ovarian Disease	100	90.0	9.0	1.0	0.0
Urogenital Disease	49	83.7	14.3	2.0	0.0
Hypertension/CHD	100	88.0	11.0	0.0	1.0
Benign Endometrial	25	84.0	8.0	4.0	4.0

In this study, 94.4% of the healthy female subjects had CA 125 II assay values at or below 35.0 U/mL (mean = 16.4, SD = 13.0). It is recommended that each laboratory establish its own reference value for the population of interest.

Monitoring of Disease Status in Patients Diagnosed with Ovarian Cancer

Changes observed in serial CA 125 assay values when monitoring ovarian cancer patients should be evaluated in conjunction with other clinical methods used for monitoring ovarian cancer patients.

The effectiveness of the ARCHITECT CA 125 II assay as an aid in the monitoring of disease status in ovarian cancer patients was determined by assessing changes in CA 125 levels in serial serum samples from 63 patients compared to changes in disease status. A study involving a total of 306 observations was performed with an average number of 4.9 observations per patient. A significant change in CA 125 level was defined as at least a 10.75% increase in assay value [i.e., 2.5 times greater than the assay's total %CV (4.3%)]. Seventy-seven percent (77% or 85/111) of the positive patient samples correlated with disease progression while sixty-one percent (61% or 81/132) of serial samples showing no significant change in CA 125 assay value correlated with no progression. The total concordance in this study was sixty-eight percent (68% or 166/243). The following table presents the data in a 2 x 2 classification scheme.

Change in Disease State per Sequential Pair

Change in CA 125 Concentration	Progression	No Progression	Total
≥ 10.75%	85	51	136
< 10.75%	26	81	107
Total	111	132	243

The following table provides the per patient distribution. Ninety-eight percent (98% or 46/47) of the significantly increased serial samples per patient correlated with disease progression while thirty-eight percent (38% or 6/16) of serum sets showing no significant change in CA 125 level correlated with no progression. The total concordance in this study was eighty-three percent (83% or 52/63).

Change in Disease State per Patient

Change in CA 125 Concentration	Progression	No Progression	Total
≥ 10.75%	46	10	56
< 10.75%	1	6	7
Total	47	16	63

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT CA 125 II assay precision is ≤ 10% total CV. A study was performed as described per the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Protocol EP5-A.[41] Three defibrinated plasma-based panels were assayed, 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.*

	Reagent			Mean Conc.	Within Run		Total	
Sample	Lot	Instrument	n	(U/mL)	SD	%CV	SD	%CV
Panel 1	1	1	80	43.5	1.1	2.4	1.7	3.9
	2	2	80	49.7	0.8	1.5	0.8	1.7
Panel 2	1	1	80	303.3	9.8	3.2	11.9	3.9
	2	2	80	340.7	5.6	1.7	6.7	2.0
Panel 3	1	1	80	598.0	18.8	3.1	25.8	4.3
	2	2	80	678.3	12.4	1.8	13.5	2.0

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

Recovery

The ARCHITECT CA 125 II assay mean recovery is 100 ± 15%. A study was performed based on guidance from Tietz Textbook of Clinical Chemistry[42] for the ARCHITECT CA 125 II assay. Known concentrations of OC 125 defined antigen were added to normal human serum samples. The concentration of CA 125 was determined using the ARCHITECT CA 125 II 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)	OC 125 Defined Antigen Added (U/mL)	Observed CA 125 Assay Value (U/mL)	% Recovery[a]
1	36.8	165	193.7	96
		715	704.7	94
2	31.3	165	160.2	82
		715	618.6	83
3	40.2	165	186.5	91
		715	695.8	92

Average Recovery across two separate spiked concentrations shown above = 90%

$$^{a}\ \%\ \text{Recovery} = \frac{\text{Observed CA 125 Conc. (U/mL)}}{\text{Endogenous CA 125 Conc. (U/mL)} + \text{CA 125 Added (U/mL)}} \times 100$$

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

Dilution Linearity

The ARCHITECT CA 125 II assay mean dilution linearity is 100 ± 15%. A study was performed for the ARCHITECT CA 125 II assay modeled after the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Protocol EP6-P2.[43] Samples with known elevated CA 125 concentrations were diluted with Multi-Assay Manual Diluent. The CA 125 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[a]
1	Undiluted	846.4	846.4	—
	1:1.4	604.6	631.4	104.4
	1:2	423.2	468.2	110.6
	1:3.3	256.5	282.8	110.3
	1:5	169.3	182.8	108.0
	1:10	84.6	92.7	109.5
	1:20	42.3	46.0	108.7
2	Undiluted	903.8	903.8	—
	1:1.4	645.6	631.6	97.8
	1:2	451.9	446.4	98.8
	1:3.3	273.9	274.0	100.1
	1:5	180.8	186.7	103.3
	1:10	90.4	95.4	105.5
	1:20	45.2	47.5	105.0
3	Undiluted	935.3	935.3	—
	1:1.4	668.1	645.9	96.7
	1:2	467.7	450.4	96.3
	1:3.3	283.4	284.7	100.5
	1:5	187.1	185.6	99.2
	1:10	93.5	95.8	102.4
	1:20	46.8	50.0	106.9

Average recovery across the three diluted samples above = 103.6%

[a] $\% \text{ Recovery} = \frac{\text{Values Obtained x Dilution Factor}}{\text{Undiluted Concentration}} \times 100$

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

Analytical Sensitivity

The sensitivity of the ARCHITECT CA 125 II assay is ≤ 1.0 U/mL (n=24 runs, in replicates of 10). Analytical sensitivity corresponds to the upper limit of the 95% confidence interval and represents the lowest concentration of OC 125 defined antigen that can be distinguished from zero.

Analytical Specificity

The ARCHITECT CA 125 II mean assay specificity is ≤ 12%. Recovery studies were performed to compare sera containing the following compounds at the indicated concentrations with control sera.*

INTERFERING SUBSTANCE

Test Compound	Test Concentration
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein	12 g/dL
Triglycerides	3 g/dL

CHEMOTHERAPEUTIC AGENTS

Test Compound	Test Concentration
Carboplatin	500 µg/mL
Cisplatin	165 µg/mL
Clotrimazole	0.3 µg/mL
Cyclophosphamide	500 µg/mL
Dexamethasone	10 µg/mL
Doxorubicin	1.16 µg/mL
Leucovorin	2.68 µg/mL
Melphalan	2.8 µg/mL
Methotrexate	45 µg/mL
Paclitaxel	3.5 ng/mL

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

POTENTIALLY INTERFERING CLINICAL CONDITIONS

The ARCHITECT CA 125 II assay was evaluated using specimens with HAMA and Rheumatoid Factor (RF) to further assess the assay specificity. Five specimens positive for HAMA and five specimens positive for RF were evaluated for % recovery with OC 125 defined antigen spiked into each specimen at 35 and 250 U/mL; mean % recovery results are summarized in the following table.*

Clinical Condition	Number of Specimens	Mean % Recovery
HAMA	10	96
RF	10	97

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

High Dose Hook

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For the ARCHITECT CA 125 II assay, no high dose hook effect was observed when samples containing up to approximately 180,000 U/mL of OC 125 defined antigen were assayed.

Method Comparison

The ARCHITECT CA 125 II assay method comparison correlation coefficient is ≥ 0.90 and the slope is 1.0 ± 0.15 for the full range of the assay. The ARCHITECT CA 125 II assay was compared to the Abbott AxSYM CA 125 assay. The results of the specimen testing are shown in the following table.*

ARCHITECT CA 125 II vs. Abbott AxSYM CA 125				
Regression Method	n	Slope (99% CI)	Intercept (99% CI)	Correlation Coefficient
Passing-Bablok †	279**	1.06 (1.03 to 1.11)	4.0 (2.0 to 4.9)	0.985
	167***	1.23 (1.16 to 1.30)	0.4 (-0.9 to 1.8)	0.967

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

** Sample Range: 4.5 - 4085.9 U/mL (ARCHITECT); 2.7 - 3436.1 U/mL (AxSYM)

*** Sample Range: 4.5 - 110.5 U/mL (ARCHITECT); 2.7 - 95.4 U/mL (AxSYM)

† A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[44]

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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
DISTRIBUTED IN THE USA BY	Distributed in the USA by
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF 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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