SIEMENS Healthineers

CA 125II™ (CA 125II™)

Current Revision and Date[a]	Rev. 05, 2022-09	
Product Name	Atellica IM CA 125II (CA 125II)	REF 10995481 (100 tests) REF 10995482 (500 tests)
Abbreviated Product Name	Atellica IM CA 125II	
Test Name/ID	CA125	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM CA 125II CAL	REF 10995483
Optional Materials	Atellica IM Multi-Diluent 1	REF 10995637 (2-pack) REF 10995638 (6-pack) REF 10995639 (vial)
	Atellica IM CA 125II MCM	REF 10995484
Specimen Types	Serum, EDTA plasma, lithium heparin plasma	
Sample Volume	50 µL	
Measuring Interval	2.0–600.0 U/mL	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE 0197

WARNING

The concentration of CA 125 in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay for CA 125 used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining serial levels of CA 125 is changed, the laboratory must perform additional testing to confirm baseline values. The Atellica IM CA 125II assay is based on the OC 125 and M11 antibodies available through agreement with Fujirebio Diagnostics, Inc. Assays using antibodies other than OC 125 and M11 may give different results.

Intended Use

The Atellica® IM CA 125II™ (CA 125II) assay is for *in vitro* diagnostic use in the quantitative, serial determination of CA 125 in human serum and plasma (EDTA and lithium heparin) and to aid in the management of patients with ovarian carcinoma using the Atellica® IM Analyzer.

The test is intended for use as an aid in monitoring patients previously treated for ovarian cancer. Serial testing for CA 125 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the Atellica IM CA 125II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or for use on any other system.

Summary and Explanation

CA 125 is identified as a 200 to 1000 kDa mucin-like glycoprotein.[1,2] CA 125 is a surface antigen associated with nonmucinous epithelial ovarian cancer.[1-3] The protein is sloughed or secreted from the surface of the ovarian cancer cells into the serum or ascites.[4] The antigen reacts to a murine monoclonal antibody, OC 125, that was originally developed by immunizing mice with cells from ovarian cancer cell line OVCA 433.[3,4] Second-generation assays for CA 125 utilize both the OC 125 and M11 epitopes, yielding an improved assay range.[5-7]

CA 125 is a useful tumor marker for evaluating therapy and monitoring disease status in patients under treatment for ovarian cancer. Post-operatively, the level of CA 125 correlates with tumor bulk and is a prognostic indicator of clinical outcome.[2,8-11] It has been reported that patients with levels > 35 U/mL have the highest risk for clinical recurrence.[9,12]

It has been reported in the literature that prior to a second-look laparotomy, a patient with levels of CA 125 > 35 U/mL is very likely to have tumor present at the surgery or to have a future recurrence.[12] However, a level of CA 125 < 35 U/mL prior to a second-look operation is not definitive evidence that the patient is free from residual tumor.[11,13] Levels of CA 125 measured after a second-look operation provide strong indications of clinical outcome.[9]

Measured serially, the levels of CA 125 correspond with disease progression or regression.[9] The rate of change in CA 125 is also highly prognostic. A rapid decrease in the level of CA 125 indicates a positive response to treatment.[3,9,10] Elevated levels of CA 125 after the third course of primary chemotherapy are predictive of poor outcome.[14]

As a diagnostic tool, the level of CA 125 alone is not sufficient to determine the presence or extent of disease. Preoperative levels of CA 125 in patients with malignant pelvic masses provide no information regarding the histologic grade or diameter of the tumor mass.[3,10] In postmenopausal women, however, the level of CA 125 in combination with ultrasonography may distinguish benign from malignant pelvic masses.[15,16]

Patients with certain benign conditions, such as hepatic cirrhosis, acute pancreatitis, endometriosis, pelvic inflammatory disease, menstruation, and first trimester pregnancy, have shown elevated levels of CA 125.[1,14,17,18] Elevated levels are found in 1%–2% of healthy donors.[1,9]

Principles of the Procedure

The Atellica IM CA 125II assay is a 2-site sandwich immunoassay using direct chemiluminometric technology, which uses 2 mouse monoclonal antibodies specific for CA 125. The first antibody is directed toward the M11 antigenic domain, and is labeled with acridinium ester. The second antibody is directed toward the OC 125 antigenic domain and is labeled with fluorescein. The immunocomplex formed with CA 125 is captured with mouse monoclonal anti-fluorescein antibody coupled to paramagnetic particles in the Solid Phase.

A direct relationship exists between the amount of CA 125 present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Reagents

Material Description	Storage	Stability[a]
Atellica IM CA 125II ReadyPack® primary reagent pack **Lite Reagent** 10.0 mL/reagent pack Mouse monoclonal anti-M11 antibody (~0.15 µg/mL) labeled with acridinium ester and mouse monoclonal anti-OC 125 (~1.0 µg/mL) labeled with fluorescein in phosphate buffer; bovine serum albumin; preservatives **Solid Phase** 25.0 mL/reagent pack Mouse monoclonal anti-fluorescein antibody (~30 µg/mL) coupled to paramagnetic particles in phosphate buffer; bovine serum albumin; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 84 days
Atellica IM Multi-Diluent 1 ReadyPack ancillary reagent pack[b] 25.0 mL/pack Equine serum; sodium azide (0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM Multi-Diluent 1[b] 50.0 mL/vial Equine serum; sodium azide (0.1%); preservatives	At 2–8°C	Until expiration date on product

[a] Refer to *Storage and Stability*.

[b] Refer to *Optional Materials*

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens-healthineers.com.

The summary of safety and performance for this *in vitro* diagnostic medical device is available to the public in the European database on medical devices (EUDAMED) when this database is available and the information has been uploaded by the Notified Body. The web address of the EUDAMED public website is: https://ec.europa.eu/tools/eudamed.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM Multi-Diluent 1 in an upright position. Atellica IM Multi-Diluent 1 is stable until the expiration date on the product when stored at 2–8°C.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 84 days. Discard reagents at the end of the onboard stability interval.

Atellica IM Multi-Diluent 1 is stable onboard the system for 28 days.

Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum and plasma (EDTA and lithium heparin) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[19]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[20]
- Follow the instructions provided with your specimen collection device for use and processing.[21]
- Allow blood specimens to clot completely before centrifugation.[22]
- Keep tubes capped at all times.[22]
- Do not use samples that have been stored at room temperature for longer than 8 hours.
- Tightly cap and refrigerate specimens at 2–8°C if the assay is not completed within 8 hours.

Storing the Specimen

Freeze samples at ≤ -20°C if the sample is not assayed within 24 hours. Thoroughly mix thawed samples before using.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Preparing the Samples

This assay requires 50 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to *Dilutions*.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[22]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10995481	1 ReadyPack primary reagent pack containing Atellica IM CA 125II Lite Reagent and Solid Phase Atellica IM CA 125II master curve and test definition MC TDEF	100
10995482	5 ReadyPack primary reagent packs containing Atellica IM CA 125II Lite Reagent and Solid Phase Atellica IM CA 125II master curve and test definition MC TDEF	500

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica IM Analyzer[a]	
10995483	Atellica IM CA 125II CAL (calibrator)	2 x 2.0 mL low calibrator CAL L 2 x 2.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
10995637	Atellica IM Multi-Diluent 1 (diluent)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack DIL
10995638	Atellica IM Multi-Diluent 1 (diluent)	6 ReadyPack ancillary reagent packs containing 25.0 mL/pack DIL
10995639	Atellica IM Multi-Diluent 1 (diluent)	50.0 mL/vial DIL
10995484	Atellica IM CA 125II MCM (master curve material)	8 x 1.0 mL levels of master curve material MCM

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Lite Reagent, then incubates for 14 minutes at 37°C.
3. Dispenses 250 µL of Solid Phase, then incubates for 12 minutes at 37°C.
4. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
5. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
6. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

For automated dilutions, ensure that Atellica IM Multi-Diluent 1 is loaded in the reagent compartment.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM CA 125II assay, use the Atellica IM CA 125II CAL. Use the calibrators in accordance with the calibrator instructions for use.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	84
Pack Calibration	84
Reagent Onboard Stability	84

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Performing Quality Control

For quality control of the Atellica IM CA 125II assay, use an appropriate quality control material of known analyte concentration with at least 2 levels (low and high) at least once during each day that samples are analyzed. For assistance in identifying a quality control material, refer to *Atellica® IM Quality Control Material Supplement* available on siemens-healthineers.com.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. The system reports results in U/mL, depending on the units defined when setting up the assay.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Dilutions

The measuring interval is 2.0–600.0 U/mL. For information about dilution options, refer to the online help.

Dilute and retest samples with CA 125 levels > 600.0 U/mL to obtain accurate results.

For automated dilutions, ensure that Atellica IM Multi-Diluent 1 is loaded in the reagent compartment. Ensure that sufficient sample volume is available to perform the dilution and that the appropriate dilution factor is selected when scheduling the test, as indicated in the table below. Enter a dilution setpoint ≤ 600 U/mL.

Sample	Dilution	Sample Volume (µL)
Serum and plasma	1:10	40
Serum and plasma	1:20	40

If patient results exceed the measuring interval of the assay when using automated dilution, or if laboratory protocol requires manual dilution, manually dilute the patient sample.

For manual dilutions, perform the following actions:

- Use Atellica IM Multi-Diluent 1 (vial) to prepare a manual dilution.
- For information about ordering tests for manually diluted samples, refer to the online help.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

The following information pertains to limitations of the assay:

Note

Do not interpret levels of CA 125 as absolute evidence of the presence or the absence of malignant disease. Before treatment, patients with confirmed ovarian carcinoma frequently have levels of CA 125 within the range observed in healthy individuals. Elevated levels of CA 125 can be observed in patients with nonmalignant diseases. Measurements of CA 125 should always be used in conjunction with other diagnostic procedures, including information from the patient's clinical evaluation.

The concentration of CA 125 in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods, calibration, and reagent specificity. CA 125 determined with different manufacturers' assays will vary depending on the method of standardization and antibody specificity. Therefore, it is important to use assay-specific values to evaluate quality control results.

- CA 125II assay testing is not recommended as a screening procedure to diagnose cancer in the general population.
- Do not use samples that contain fluorescein. Evidence suggests that patients undergoing retinal fluorescein angiography can retain amounts of fluorescein in the body for up to 72 hours post-treatment. In the cases of patients with renal insufficiency, including many diabetics, retention could be longer. Such samples can produce either falsely elevated or falsely depressed values when tested with this assay, and should not be tested.[23]
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[24,25]

Expected Values

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur® system. Expected values were established using the ADVIA Centaur system and confirmed by assay comparison. Refer to *Assay Comparison*.

Results were obtained on 239 apparently healthy women. In this study, 1% of the women had CA 125 levels > 35 U/mL. The median age of the women was 48 years of age (range: 17–79 years). The Upper Limit of Normal (ULN) for this group, defined as the 97.5th percentile of the observed results, was established at 30.2 U/mL.

Additional data was generated on patient samples, as shown in the following table:

Sample Category	N	% of Patients with levels of CA 125 > 35 U/mL
Normals		
Premenopausal women	100	2
Postmenopausal women	99	0
Pregnancy	15	13.3
Benign disease		
Cervical displasia	20	20
Endometriosis	10	10
Uterine fibroids	10	20
Ovarian cysts	10	0
Pelvic inflammatory disease	10	0
Polycystic ovaries	10	40

Sample Category	N	% of Patients with levels of CA 125 > 35 U/mL
Malignant disease		
Active Ovarian	116	79.3
Breast	34	32
Lymphoma	10	0
Colorectal	10	50
Lung	10	10
Prostate	10	0

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[26] Consider these values as guidance only.

Monitoring Disease and Therapy

A retrospective clinical study was conducted to evaluate CA 125 values in 44 ovarian cancer patients during the course of disease and therapy using the ADVIA Centaur system. The study group included patients who responded to therapy, experienced disease progression, exhibited stable persistent disease, and demonstrated no evidence of disease (NED). An increase of ≥ 30% in CA 125 value, with a final value > 35 U/mL, was considered an indication of disease progression. A decrease of ≥ 30% was considered an indication of response. The table below summarizes the results of the clinical study.

Longitudinal Patient Evaluation Results - Ovarian Cancer Patients Only

Correspondence (Parallels Clinical Course)	N	Percentage
Increasing CA 125II with progression	23	52
Decreasing CA 125II with response	6	14
Stable disease or no evidence of disease with no change in CA 125II values	5	11
Total paralleling clinical course	34	77
No correspondence (total) (Does not parallel clinical course)	10	23

The following table shows the correspondence of CA 125 changes to changes in the clinical status of the patient. The sensitivity of longitudinal measurements using the ADVIA Centaur system was 93.5%.

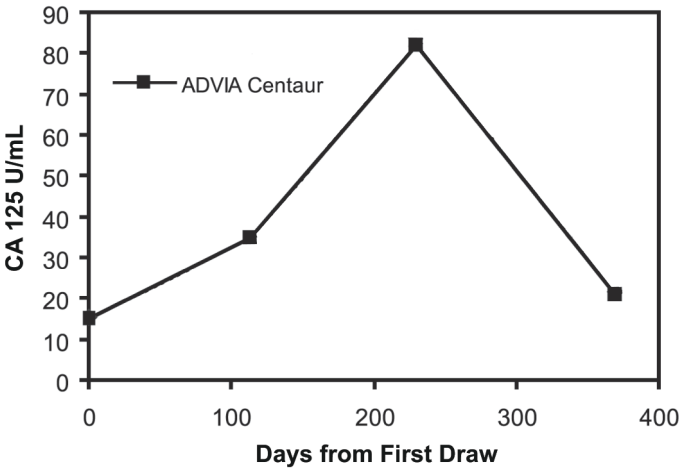
Monitoring Ovarian Cancer Patients

	ADVIA Centaur CA 125II		
Clinical Status	**Change**	**No Change**	**Total**
Change	29	8	37
No Change	2	5	7
Total	31	13	44

		95% CI
Sensitivity	93.5%	78.6%–99.2%
Specificity	38.5%	13.9%–68.4%

A representative profile of a monitored ovarian cancer patient is shown in the figure below. Results for the CA 125II assay using the ADVIA Centaur system are shown.

Ovarian Cancer Patient



Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur system. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur system.

Measuring Interval

2.0–600.0 U/mL

The lower limit of the measuring interval is defined by the analytical sensitivity. Report results below the measuring interval as < 2.0 U/mL.

When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

There are no known cross-reactants for CA 125.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[27] The assay is designed to have an analytical sensitivity of ≤ 2.0 U/mL, a limit of blank (LoB) ≤ 2.0 U/mL, a limit of detection (LoD) ≤ 3.0 U/mL, and a limit of quantitation (LoQ) ≤ 3.0 U/mL.

Representative detection capability data are shown below. Assay results obtained at individual laboratories may vary from the data presented.

Analytical sensitivity is defined as the concentration of CA 125 that corresponds to the RLUs that are 2 standard deviations more than the mean RLUs of 20 replicate determinations of the CA 125 zero standard. This response is an estimate of the minimum detectable concentration with 95% confidence. The analytical sensitivity for the Atellica IM CA 125II assay is 1.2 U/mL.

The LoB corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoB of the Atellica IM CA 125II assay is 1.1 U/mL.

The LoD corresponds to the lowest concentration of CA 125 that can be detected with a probability of 95%. The LoD for the Atellica IM CA 125II assay is 3.0 U/mL, and was determined using 159 determinations, with 79 blank and 80low- level replicates, and an LoB of 1.1 U/mL.

The LoQ corresponds to the lowest amount of cancer antigen CA 125 in a sample at which the within laboratory CV is ≤ 20%. The LoQ of the Atellica IM CA 125II assay is 3.0 U/mL, and was determined using multiple patient samples in the interval 0.1–37.9 U/mL.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[28] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The assay was designed to have within-laboratory precision of ≤ 2.1 SD for samples ≤ 30.0 U/mL and ≤ 7.0% CV for samples from 30.0–600.0 U/mL. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (U/mL)	SD[b] (U/mL)	CV[c] (%)	SD (U/mL)	CV (%)
Serum A	80	15.1	0.2	N/A[d]	0.4	N/A
Serum B	80	49.4	0.9	1.8	1.5	3.1
Serum C	80	172.9	2.5	1.4	4.9	2.8
Serum D	80	288.0	4.7	1.6	8.7	3.0
Serum E	80	519.0	7.2	1.4	16.5	3.2
Control 1	80	32.8	0.5	1.5	0.9	2.7
Control 2	80	78.7	2.2	2.8	2.7	3.4
Control 3	80	215.5	6.0	2.8	7.6	3.5

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.
[d] Not applicable.

Based on internal testing on the Atellica IM Analyzer, the overall reproducibility is estimated to be ≤ 8% CV for samples tested and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Assay Comparison

The Atellica IM CA 125II assay is designed to have a correlation coefficient of ≥ 0.95 and a slope of 1.0 ± 0.1 compared to the ADVIA Centaur CA 125II assay. Assay comparison was determined using the weighted Deming regression model in accordance with CLSI Document EP09-A3.[29] The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Centaur CA 125II	y = 0.99x + 1.7 U/mL	10.2–566.8 U/mL	115	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

Agreement of the assays may vary depending on the study design, comparative assay, and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Specimen Equivalency

Specimen equivalency was determined with the Deming linear regression model in accordance with CLSI Document EP09-A3.[29] The following results were obtained:

Tube (y) vs. Serum (x)	N[a]	Sample Interval	Slope	Intercept	r[b]
Dipotassium EDTA plasma	156	3.0–587.7 U/mL	0.98	-0.9 U/mL	1.00
Lithium heparin plasma	115	3.3–573.4 U/mL	1.05	0.1 U/mL	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

The assay is designed to have a slope of 0.90–1.10 for alternate tube types versus serum.

Agreement of the specimen types may vary depending on the study design and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP7-A2.[30]

The potential interference of chemotherapeutic agents, therapeutic drugs, and tumor marker antigens was tested by adding these substances to serum pools containing 35 U/mL CA 125. The level of CA 125 in each of these pools was then determined and percent recovery relative to the pool without the potential interference was calculated.

Substance	Amount Added (µg/mL)	Mean % Recovery (Spike/Control x 100)
5-Fluorouracil	1	101
Cis-Platinum	175	95
Cyclophosphamide (Cytoxan)	800	97
Diethylstilbesterol	25	100
Doxorubicin (Adriamycin)	50	104
Etoposide	10	102
Flutamide	10	99
Megesterol acetate	10	99
Mitomycin	75	101
Methotrexate	450	97
Tamoxifen	60	101
Vincristine	1.5	99

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Substance	Substance Test Concentration	Bias (%)
Conjugated Bilirubin	20 mg/dL	-6.8
Unconjugated Bilirubin	20 mg/dL	2.4
Triglycerides	900 mg/dL	-5.7

Substance	Substance Test Concentration	Bias (%)
Hemoglobin	1000 mg/dL	0.7
Albumin	6.5 g/dL	-2.2
Cholesterol	500 mg/dL	7.8

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Interference testing was performed using the ADVIA Centaur XP system in accordance with CLSI Document EP07-ed3.[31] The following results were obtained:

Substance	Substance Test Concentration	Analyte Concentration (U/mL)	Bias (%)
Dipotassium EDTA	9.0 mg/mL	39.6	3.7
		526.5	1.3
Heparin	75 U/mL	42.4	3.2
		471.4	-0.9

Assay results obtained at individual laboratories may vary from the data presented.

Dilution Recovery

A total of 6 samples with concentrations of CA 125 in the range of 472.6–795.8 U/mL were diluted 1:2, 1:4, 1:8, and 1:16 with Multi-Diluent 1 and assayed for recovery and parallelism. The recoveries ranged from 85.3%–112.5% with a mean of 98.5%.

Note Sample-dependent nonlinear dilutions can be observed.[32]

Sample	Dilution	Observed (U/mL)	Expected (U/mL)	Recovery %
1	—	640.2	—	—
	1:2	340.1	320.1	106.2
	1:4	160.7	160.0	100.4
	1:8	80.1	80.0	100.1
	1:16	40.0	40.0	99.9
	Mean			101.7
2	—	795.8	—	—
	1:2	425.7	397.9	107.0
	1:4	216.5	199.0	108.8
	1:8	109.5	99.5	110.0
	1:16	56.0	49.7	112.5
	Mean			109.6
3	—	511.1	—	—
	1:2	238.8	255.6	93.4

Sample	Dilution	Observed (U/mL)	Expected (U/mL)	Recovery %
	1:4	118.0	127.8	92.3
	1:8	59.6	63.9	93.4
	1:16	30.6	31.9	95.7
	Mean			93.7
4	—	612.1	—	—
	1:2	314.4	306.1	102.7
	1:4	148.0	153.0	96.7
	1:8	70.6	76.5	92.2
	1:16	36.8	38.3	96.2
	Mean			97.0
5	—	472.6	—	—
	1:2	227.8	236.3	96.4
	1:4	121.6	118.1	102.9
	1:8	59.3	59.1	100.4
	1:16	30.7	29.5	103.9
	Mean			100.9
6	—	497.8	—	—
	1:2	219.2	248.9	88.1
	1:4	110.4	124.5	88.7
	1:8	56.2	62.2	90.4
	1:16	26.5	31.1	85.3
	Mean			88.1
Mean				98.5

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Spiking Recovery

Various amounts of CA 125 were added to 6 serum samples with endogenous CA 125 levels ranging from 6.6–20.6 U/mL. The recoveries ranged from 83.7%–104.4% with a mean of 95.0%.

Sample	Amount Added (U/mL)	Observed (U/mL)	Recovery %
1	—	20.6	—
	492	473.3	96.1
	270	235.1	87.2

Sample	Amount Added (U/mL)	Observed (U/mL)	Recovery %
	135	126.8	93.8
	67	62.2	92.6
	37	31.1	84.9
	Mean		90.9
2	—	6.6	—
	492	504.5	102.5
	270	263.8	97.9
	135	140.6	104.1
	67	70.0	104.4
	37	35.6	97.3
	Mean		101.2
3	—	10.8	—
	492	471.2	95.7
	270	259.8	96.4
	135	132.5	98.0
	67	66.5	99.1
	37	34.6	94.5
	Mean		96.7
4	—	14.0	—
	492	430.5	87.4
	270	233.0	86.5
	135	123.4	91.3
	67	61.3	91.3
	37	30.6	83.7
	Mean		88.0
5	—	9.1	—
	492	463.5	94.1
	270	250.4	92.9
	135	131.5	97.2
	67	65.3	97.4
	37	34.0	93.0
	Mean		94.9
6	—	9.3	—

Sample	Amount Added (U/mL)	Observed (U/mL)	Recovery %
	492	470.4	95.6
	270	266.1	98.7
	135	132.7	98.2
	67	69.4	103.5
	37	34.8	95.1
	Mean		98.2
Mean			95.0

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

High-Dose Hook Effect

High CA 125 concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with CA 125 concentrations as high as 70,000 U/mL will report > 600 U/mL. Results were established using the Atellica IM Analyzer.

Standardization

The Atellica IM CA 125II assay standardization is traceable to an internal standard manufactured using highly purified material. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

For customer support, contact your local technical support provider or distributor.

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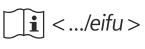
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]		Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]		Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]		Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
 < .../eifu >	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
	*In vitro* diagnostic medical device	5.5.1[a]		Revision	Proprietary
RxOnly	Prescription device (US only)	FDA[b]		Unique Device Identifier	5.7.10[c]
	CE Marking with Notified Body	EU IVDR[d]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
UNITS C	Common Units	Proprietary	UNITS SI	International System of Units	Proprietary
YYYY-MM-DD	Date format (year-month-day)	N/A	YYYY-MM	Date format (year-month)	N/A
	Document face up[f]	1952[e]		Handheld barcode scanner	Proprietary
	Target	Proprietary		Mixing of substances	5657[g]
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary		Interval	Proprietary
MATERIAL ID	Unique material identification number	Proprietary	MATERIAL	Material	Proprietary
CONTROL TYPE	Type of control	Proprietary	CONTROL NAME	Name of control	Proprietary
CONTROL LOT VAL	Quality control lot value	Proprietary	CAL LOT VAL	Calibrator lot value	Proprietary

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.
[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.
[c] ISO 15223-1:2020-04
[d] IVDR REGULATION (EU) 2017/746
[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.
[f] Indicates Assay-eNote
[g] International Electrotechnical Commission (IEC). IEC 60417-1 Graphical symbols for use on equipment – Part 1: Overview and Application

Legal Information

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