Squamous Cell Carcinoma (SCC)

Current Revision and Date[a]	Rev. 02, 2022-06		
Product Name	ADVIA Centaur Squamous Cell Carcinoma (SCC)	REF	11354594 (100 tests)
Abbreviated Product Name	ADVIA Centaur SCC		
Test Name/ID	SCC		
Systems	ADVIA Centaur CP system		
Materials Required but Not Provided	ADVIA Centaur Squamous Cell Carcinoma Calibrator (SCC CAL)	REF	11553960
	ADVIA Centaur Wash 1 (2 × 1500 mL)	REF	01137199 (112351)
	ADVIA Centaur Wash 1 (2 × 2500 mL)	REF	03773025
Optional Materials	ADVIA Centaur Tumor Marker Quality Control (TM QC)	REF	11538186
	ADVIA Centaur Multi-Diluent 13	REF	10492364
Specimen Types	Serum, EDTA plasma		
Sample Volume	50 µL		
Measuring Interval	0.60–70.00 ng/mL (0.60–70.00 µg/L)		

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

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WARNING

The concentration of SCC 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 SCC assay 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 SCC is changed, the laboratory must perform additional testing to confirm baseline values.

WARNING

SCC reactive determinants are shed naturally in saliva and other bodily fluids. Contamination of the samples or assay materials may cause falsely elevated SCC assay values.

Intended Use

The ADVIA Centaur® Squamous Cell Carcinoma (SCC) assay is for *in vitro* diagnostic use in the quantitative measurement of squamous cell carcinoma (SCC) antigen in human serum and plasma (EDTA) using the ADVIA Centaur® CP system.
The assay is used as an aid in the management of patients with squamous cell carcinoma. The measurement of SCC antigen, in conjunction with other clinical and laboratory findings, is used as an aid in monitoring disease progression during the course of disease and treatment in squamous cell carcinoma in lung, cervical, and head and neck cancer patients. Serial testing for patient SCC assay values should be used in conjunction with other clinical methods used for monitoring lung cancer.

Summary and Explanation

Squamous Cell Carcinoma Antigen (SCC Ag) is a 42 kDa subfraction of tumor-antigen-4 (TA-4), a glycoprotein with a molecular weight of approximately 48 kDa and multiple subfractions. The SCC Ag subfraction is a tumor marker extracted from squamous cell carcinomas of the uterine cervix.[1] The gene for SCC Ag encodes two antigens, SCC Ag1 and SCC Ag2, both detectable in serum.[2,3] These antigens, present in the cytosol, are released into the bloodstream and may be elevated in patients with squamous cell carcinoma. SCC Ag1 and SCC Ag2 are co-expressed in the lung, head and neck, as well as the squamous epithelium of tongue, tonsils, esophagus, uterine cervix, and vagina.[4]

SCC Ag has been studied in squamous cell malignancies of the lung, esophagus, head and neck, anal canal, and skin. It has been reported that rising antigen in serial determinations may indicate disease recurrence. Measurement of SCC Ag levels has been used to monitor residual disease post treatment as well as response to therapy. More advanced cancer stages are associated with higher SCC Ag levels.[5-11]

SCC Ag has specifically been reported as a biomarker for non-small cell lung cancer (NSCLC), primarily of the squamous cell carcinoma type. In NSCLC, SCC Ag has been used to monitor disease recurrence and residual disease following treatment and response to therapy.

SCC Ag is often used as a biomarker for cervical cancer and is recognized as the marker of choice for the follow-up of cervical cancer according to the European Group of Tumor Markers guidelines.[12] Elevated SCC Ag is associated with radiotherapy resistance and studies have demonstrated that the rate of SCC Ag reduction during radiotherapy can predict tumor response after treatment.[13] Moreover, failure of SCC Ag levels to normalize posttreatment have been shown to predict tumor relapse with a high specificity.

Squamous cell-based cancers represent a significant number of head and neck cancers originating from the mucosal lining (epithelium) of these regions. Various studies have shown that SCC Ag is a significant independent predictor of disease-free survival and pretreatment levels are an independent prognostic indicator in these patients.

Principles of the Procedure

The ADVIA Centaur SCC assay is a fully automated, 2-site sandwich immunoassay using direct chemiluminescent technology. The Solid Phase contains magnetic microparticles coated with anti-SCC107 mouse monoclonal antibody. The Lite Reagent consists of acridinium ester-labeled anti-SCC140 mouse monoclonal antibody.

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

Reagents

Material Description	Storage	Stability
ADVIA Centaur SCC ReadyPack® primary reagent pack[a,b] **Lite Reagent** 10.0 mL/reagent pack Anti-SCC monoclonal antibody covalently labeled with acridinium ester (~0.75 µg/mL) in buffer containing bovine serum albumin; surfactant; preservatives **Solid Phase** 17.5 mL/reagent pack Anti-SCC monoclonal antibody (< 0.001%) covalently coupled to magnetic microparticle in buffer containing bovine serum albumin; surfactant; preservatives	Unopened at 2–8° C Onboard	Until expiration date on product 30 days
ADVIA Centaur Multi-Diluent 13 ReadyPack ancillary reagent pack[a,b,c] 2 x 10.0 mL/pack Buffer; surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C Onboard	Until expiration date on product 28 days
ADVIA Centaur Wash 1[a,d] 2 x 1500 mL/pack Phosphate-buffered saline; sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month
ADVIA Centaur Wash 1[a,d] 2 x 2500 mL/pack Phosphate-buffered saline; sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month

[a] Store in an upright position.
[b] Prevent exposure to sunlight and heat.
[c] Refer to Optional Materials.
[d] Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

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

H317	**Warning!**
H319	May cause an allergic skin reaction.
H412	Causes serious eye irritation.
P261, P280,	Harmful to aquatic life with long lasting effects.
P273,	Avoid breathing vapor. Wear protective gloves/protective clothing/eye
P302+P352,	protection/face protection. Avoid release to the environment. IF ON
P305+P351+	SKIN: Wash with plenty of soap and water. IF IN EYES: Rinse cautiously
P338	with water for several minutes. Remove contact lenses, if present and
P333+P313,	easy to do. Continue rinsing. If skin irritation or rash occurs: Get medical
P362+P364,	advice/attention. Take off contaminated clothing and wash it
P501	before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
	Contains: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1) (ADVIA Centaur SCC Solid Phase and Lite Reagent).

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (EDTA) are the recommended specimen types for this assay.

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.

Collecting the Specimen

- Wear proper protective gear, including gloves and a face mask, to ensure SCC will not be shed into the specimen.
- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[14]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[15]
- Follow the instructions provided with your specimen collection device for use and processing.[16]
- Allow blood specimens to clot completely before centrifugation.[17]
- Keep tubes capped at all times.[17]

Storing the Specimen

- Uncentrifuged specimens are stable under the following conditions:
  - Serum and tripotassium EDTA plasma in the primary collection device are stable for up to 3 days at 2–8° C.
  - Dipotassium EDTA plasma is unstable if left unprocessed. Do not delay centrifugation.
- After centrifugation, specimens left in the primary collection tube in contact with the cells or on the clot are stable under the following conditions:
  - Serum samples are stable for up to 4 days at room temperature, and for up to 4 days at 2–8° C.
  - Plasma samples are stable for up to 1 day at room temperature, and for up to 1 day at 2–8° C.
- Separated samples are stable under the following conditions:
  - Red Top serum samples are stable for up to 7 days at room temperature, and for up to 1 month at 2–8° C.
  - SST serum samples are stable for up to 7 days at room temperature, and for up to 1 day at 2–8° C.
  - Plasma samples are stable for up to 7 days at room temperature, and for up to 1 month at 2–8° C.
  - All samples are stable at ≤ -10° C for up to 1 month. Avoid more than 1 freeze-thaw cycle. Do not store in a frost-free freezer. Thoroughly mix thawed samples and centrifuge them before using.

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.

If during shipment, specimens may be subjected to temperatures > 25° C, then ship specimens frozen.

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 a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

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

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

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[17]

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11354594	1 ReadyPack primary reagent pack containing ADVIA Centaur SCC Lite Reagent and Solid Phase	100
	ADVIA Centaur SCC master curve and test definition MC TDEF	

Materials Required but Not Provided

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

REF	Description
	ADVIA Centaur CP System[a]
11553960	ADVIA Centaur SCC CAL (calibrator) CAL LOT VAL
01137199 (112351)	ADVIA Centaur Wash 1 (wash) WASH 1
03773025	ADVIA Centaur Wash 1 (wash) WASH 1

[a] Additional system fluids are required to operate the system: ADVIA Centaur Acid Reagent, ADVIA Centaur Base Reagent, and ADVIA Centaur Cleaning Solution.

Optional Materials

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

REF	Description
11538186	ADVIA Centaur TM QC (quality controls) CONTROL LOT VAL
10492364	ADVIA Centaur Multi-Diluent 13 (diluent) DIL

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 175 µL of Solid Phase, then incubates for 6 minutes at 37° C.
3. Dispenses 100 µL of Lite Reagent, then incubates for 6 minutes at 37° C.
4. Performs a wash sequence using ADVIA Centaur Wash 1.
5. Dispenses 300 µL each of ADVIA Centaur Acid Reagent and ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
6. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided, Materials Required but Not Provided,* and *Optional Materials* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve values by scanning the master curve card. For information about defining the master curve, refer to the system online help.

Performing Calibration

For calibration of the ADVIA Centaur SCC assay, use ADVIA Centaur SCC 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:

- At the end of the 30-day calibration interval.
- When changing lot numbers of primary reagent packs.

- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

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 ADVIA Centaur SCC assay, use the ADVIA Centaur TM QC or an equivalent product at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided.

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 expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system online help.

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system online help. The system reports results in ng/mL (common units) or µg/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: 1 ng/mL = 1 µg/L

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

Dilutions

The measuring interval is 0.60–70.00 ng/mL (0.60–70.00 µg/L). For information about dilution options, refer to the system online help.

Dilute and retest samples with SCC levels > 70.00 ng/mL (70.00 µg/L) to obtain accurate results.

For automated dilutions, perform the following activities:

- Load ADVIA Centaur Multi-Diluent 13.
- Ensure that sufficient sample volume is available. Refer to the table below.
- Select the appropriate dilution factor.

For automatic dilutions enter a Dilution Point ≤ 70 ng/mL (70 µg/L).

Sample	Dilution	Sample Volume (µL)
Serum and plasma	1:10	50

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:

- Do not perform manual dilution.
- Dipotassium EDTA plasma is unstable if left unprocessed. Do not delay centrifugation.
- Do not use Lithium Heparin plasma tubes.
- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' SCC methods.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[18,19] Additional information may be required for diagnosis.

Expected Values

Expected values were established using the ADVIA Centaur XPT system and confirmed by assay comparison. Refer to *Assay Comparison*.

A reference interval for healthy adults (smokers and nonsmokers) was established in accordance with CLSI Document EP28-A3c[20] on the ADVIA Centaur XPT system.

Samples tested were a combination of commercially available samples (N=14) and samples collected prospectively from apparently healthy subjects (N=226), males and females ≥ 22

years old without any chronic medical conditions or on chronic-use medications, women using hormones for menopause or on birth control were eligible. The reference interval was determined by calculating the 95th and 97.5th percentiles of the distribution of values.

		Median	Reference Interval
Group	**N[a]**	**ng/mL or µg/L**	**Percentile (CI)**
Adults (22–87 years)	240	1.24	2.86 (2.61 – 3.13)[b] 3.35 (3.01 – 3.71)[c]
Smoker (22–73 years)	120	1.26	3.06 (2.66 – 3.47)[b] 3.61 (3.11 – 4.20)[c]
Nonsmoker (22–87 years)	120	1.21	2.71 (2.39 – 3.06)[b] 3.17 (2.70 – 3.72)[c]

[a] Number of samples tested.
[b] 95th percentile
[c] 97.5th percentile

The distribution in percentage (%) of SCC assay values in benign and malignant cohorts was determined using 829 serum samples obtained from 9 U.S-based clinical centers and commercially available sources using the ADVIA Centaur SCC assay.

		Percentage ≥ 2.86 ng/mL	**Mean**	**SD**	**25th Percentile**	**Median**	**75th percentile**
Group	**N[a]**	**(%)**	**ng/mL or µg/L**	**ng/mL or µg/L**	**ng/mL or µg/L**	**ng/mL or µg/L**	**ng/mL or µg/L**
Benign Conditions							
Lung Diseases	75	18.7	2.27	2.64	1.05	1.43	2.43
Breast Diseases	37	0.0	1.01	0.36	0.74	0.92	1.31
Liver Diseases	38	2.6	1.39	0.61	0.83	1.34	1.76
Renal Diseases	39	30.8	3.72	3.96	1.23	2.18	4.39
Benign Prostatic Hyperplasia	40	17.6	3.06	4.70	1.24	1.81	2.67
Cancer							
Treatment-naive NSCLC	120	2.5	1.34	0.95	0.76	1.17	1.69
Bladder	40	20.0	2.87	3.59	1.12	1.77	2.53
Breast	48	2.1	1.23	0.77	0.77	0.96	1.60
Cervical	40	35.0	8.21	15.34	1.06	1.58	5.28
Colorectal	40	15.0	2.75	6.74	0.98	1.42	2.17
Esophageal SCC	35	28.6	2.78	1.88	1.45	2.07	3.43
Head & Neck	40	15.0	4.22	12.56	1.12	1.53	2.22

Group	N[a]	Percentage ≥ 2.86 ng/mL (%)	Mean ng/mL or µg/L	SD ng/mL or µg/L	25th Percentile ng/mL or µg/L	Median ng/mL or µg/L	75th percentile ng/mL or µg/L
Neuroendocrine	37	10.8	1.43	0.78	0.97	1.19	1.59
Ovarian	40	5.0	1.39	1.46	0.71	0.91	1.55
Prostate	40	12.5	1.72	1.19	0.92	1.39	1.97
Renal	40	20.0	2.59	3.80	1.23	1.90	2.56
Stomach	40	5.0	1.50	1.04	0.91	1.22	1.68
Testicular	40	7.5	1.54	0.87	0.86	1.37	1.94

[a] Number of samples tested.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[20] Consider these values as guidance only.

Performance Characteristics

Measuring Interval

0.60–70.00 ng/mL (0.60–70.00 µg/L)

The lower limit of the measuring interval is defined by the limit of quantitation (LoQ). Report results below the measuring interval as < 0.60 ng/mL (0.60 µg/L).

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

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[21]

Method	Result ng/mL or µg/L
Limit of Blank (LoB)	0.18
Limit of Detection (LoD)	0.34
Limit of Quantitation (LoQ)	0.34

These are representative data and the assay results obtained at individual laboratories may vary from the data presented.

The LoB corresponds to the highest measurement result likely to be observed for a blank sample with a probability of 95%. The assay was designed to have an LoB of < 0.60 ng/mL (0.60 µg/L).

The LoD corresponds to the lowest concentration of SCC Ag that can be detected with a probability of 95%. The assay was designed to have an LoD of ≤ 0.60 ng/mL (0.60 µg/L).

The LoQ corresponds to the lowest amount of SCC Ag in a sample at which the within-laboratory precision (%CV) is ≤ 20%. The assay was designed to have an LoQ of ≤ 0.60 ng/mL (0.60 µg/L).

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[22] Samples were assayed in duplicate in 2 runs per day for 20 days.

The following results are representative of the performance of the assay:

			Repeatability		Within-Laboratory Precision	
		Mean	SD[b]	CV[c]	SD	CV
Specimen Type	N[a]	ng/mL or µg/L	ng/mL or µg/L	(%)	ng/mL or µg/L	(%)
Serum A	80	0.90	0.042	N/A[d]	0.046	N/A[d]
Serum B	80	3.20	0.087	2.7	0.198	3.1
Serum C	80	8.36	0.169	2.0	0.254	3.0
Serum D	80	38.30	0.547	1.4	1.005	2.6
Serum E	80	66.00	1.137	1.7	1.332	2.0

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

The assay was designed to have the following precision.

Concentration Interval	Precision	
ng/mL or µg/L	Repeatability (Within-Run)	Within-Laboratory (Total Precision)
≥ 3.00	≤ 7.5% CV	≤ 7.5% CV
≥ 0.41-< 3.00	≤ 0.23 ng/mL SD (≤ 0.23 µg/L SD)	≤ 0.23 ng/mL SD (≤ 0.23 µg/L SD)

Assay Comparison

Assay comparison was determined with the weighted Deming regression model in accordance with CLSI Document EP09c-ed3.[23]

Agreement of the assays may vary depending on the study design, comparative assay, and population tested.

Specimen Type	Comparative Assay (x)	Regression Equation	Sample Interval ng/mL or µg/L	N[a]	r[b]
Serum	ADVIA Centaur SCC assay using the ADVIA Centaur XPT system	y = 1.05x - 0.02 ng/mL (y = 1.05x - 0.02 µg/L)	0.55–54.61	119	0.997

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

The assay is designed to have a correlation coefficient of ≥ 0.97, a slope of 1.00 ± 0.10, and an intercept within ± 0.60 ng/mL (0.60 µg/L).

Specimen Equivalency

Specimen equivalency was determined with the weighted Deming regression model using the ADVIA Centaur XPT system in accordance with CLSI Document EP09c-ed3.[23]

Agreement of the specimen types may vary depending on the study design and population tested.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval ng/mL or µg/L	N[a]	r[b]
Dipotassium EDTA plasma	y = 1.02x + 0.08 ng/mL (y = 1.02x + 0.08 µg/L)	0.78–62.62	50	0.997
Tripotassium EDTA plasma	y = 0.98x + 0.08 ng/mL (y = 0.98x + 0.08 µg/L)	0.64–69.16	50	0.998
Serum separator tube (SST)	y = 0.99x - 0.07 ng/mL (y = 0.99x - 0.07 µg/L)	0.68–61.65	50	0.996

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

The assay is designed to have a correlation coefficient of ≥ 0.97, a slope of 1.0 ± 0.10, and an intercept within ± 0.60 ng/mL (0.60 µg/L).

Interferences

Hemolysis, Icterus, Lipemia (HIL)

Interference testing was performed using the ADVIA Centaur XPT system in accordance with CLSI Document EP07-ed3.[24]

The following substances do not interfere with the assay when present in serum at the concentrations indicated. Bias due to these substances does not exceed 10% at analyte concentrations of approximately 2.50 ng/mL (2.50 µg/L) and 50.0 ng/mL (50.0 µg/L).

Substance	Substance Test Concentration
Hemoglobin	1012 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	67 mg/dL
Lipemia (Triglycerides)	1516 mg/dL
Lipemia (Intralipid)	1500 mg/dL

Other Substances

Interference testing was performed using the ADVIA Centaur XPT system in accordance with CLSI Document EP07-ed3[24] and EP37-ed1.[25]

The following substances do not interfere with the assay when present in serum at the concentrations indicated. Bias due to these substances does not exceed 10% at analyte concentrations of approximately 2.50 ng/mL (2.50 µg/L) and 50.0 ng/mL (50.0 µg/L).

Substance	Substance Test Concentration
Total Protein	15 g/dL
Immunoglobulin G	20 g/L
Immunoglobulin A	5 g/L
Immunoglobulin M	10 g/L
Rheumatoid Factor	1003 IU/mL
Human Anti-Mouse Antibodies (HAMA IgG)	1000 µg/L
5-Fluorouracil	900 µg/mL
Acetaminophen	200 µg/mL
Acetylcysteine	553 µg/mL
Acetylsalicylic acid	1000 µg/mL
Afatinib	0.024 mg/mL
Ampicillin-Na	1000 µg/mL
Aprepitant	0.075 mg/mL
Ascorbic acid	300 µg/mL
Atezolizumab	1.008 mg/mL
Bevacizumab	700 µg/mL
Biotin	3500 ng/mL
Carboplatin	600 µg/mL
Cefoxitin	2500 µg/mL
Cetuximab	600 µg/mL
Cisplatin	180 µg/mL

Substance	Substance Test Concentration
Cyclophosphamide	500 µg/mL
Cyclosporine	5 µg/mL
Dexamethasone	20 µg/mL
Docetaxel	112.5 µg/mL
Doxorubicin	120 µg/mL
Doxycycline	50 µg/mL
Epoetin Alfa	0.378 µg/mL
Erlotinib	150 µg/mL
Etoposide	300 µg/mL
Fosaprepitant	0.09 mg/mL
Gefitinib	250 µg/mL
Gemcitabine	1500 µg/mL
Heparin	5000 U/L
Ibuprofen	500 µg/mL
Ifosfamide	7200 µg/mL
Levodopa	20 µg/mL
Methotrexate	150 µg/mL
Methyldopa +1.5	20 µg/mL
Metoclopramide	7.5 µg/mL
Metronidazole	200 µg/mL
Nab-Paclitaxel	0.06 mg/mL
Neupogen	0.9 µg/mL
Nivolumab	0.288 mg/mL
Ondansetron	0.0342 mg/dL
Paclitaxel	265 µg/mL
Palonosetron	0.00015 mg/mL
Pegfilgrastim	0.0036 mg/mL
Pembrolizumab	0.24 mg/mL
Phenylbutazone	400 µg/mL
Prochlorperazine	0.345 mg/dL
Rifampicin	60 µg/mL
Theophylline	100 µg/mL
Topotecan hydrochloride	2.25 µg/mL
Vincristine sulfate	3 µg/mL
Vinorelbine tartrate	53.1 µg/mL

Cross-Reactivity

Cross-reactivity was determined using the ADVIA Centaur XPT system in accordance with CLSI Document EP07-ed3.[24]

Cross-reactant	Cross-reactant Concentration	SCC concentration (ng/mL or µg/L)	Cross-reactivity (%)
ProGRP[a]	1900 ng/L	2.50 50.00	8 21
CA 125	950 U/mL	2.50 50.00	< 1 < 1
NSE	400 ng/mL	2.50 50.00	< 1 < 1
CYFRA 21-1	100 ng/mL	2.50 50.00	< 1 1
CEA	70 µg/L	2.50 50.00	< 1 2

[a] Due to the extremely low concentration, cross reactivity for ProGRP can appear unusually high. The Percent Difference for ProGRP ranged from 0% to 7%.

Linearity

Linearity testing was performed in accordance with CLSI Document EP06-ed2.[26]

Linearity was evaluated using a sample that contained a high level of SCC, mixed in various proportions with a sample that contained a low level of SCC. The resulting sample mixtures (15 combinations) were assayed for SCC.

The ADVIA Centaur SCC assay is linear for the measuring interval of 0.60–70.00 ng/mL (0.60–70.00 µg/L).

Onboard Dilution Recovery

Serum samples were diluted onboard the ADVIA Centaur CP system with ADVIA Centaur Multi-Diluent 13.

The following results are representative of the performance of the assay:

		Observed	Expected	Recovery
Sample	**Dilution**	**ng/mL or µg/L**	**ng/mL or µg/L**	**(%)**
1	1:10	82.54	85	97
2	1:10	190.69	200	95
3	1:10	348.93	350	100
4	1:10	507.28	500	101
5	1:10	658.90	650	101
Mean				99

High-Dose Hook Effect

High SCC concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with SCC concentrations above the measuring interval and as high as 5,000 ng/mL (5,000 µg/L) will report >70.00 ng/mL (70.00 µg/L).

Standardization

The ADVIA Centaur SCC assay is traceable to an internal standard manufactured using highly purified material.

Currently no reference standard is available for this assay.

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.

siemens-healthineers.com

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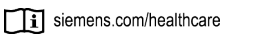
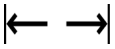
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
 	Internet URL address to access the electronic instructions for use
	Revision
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive
	Dangerous to environment

Symbol	Symbol Title and Description
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Do not freeze.
	Handheld barcode scanner
IVD	*In vitro* diagnostic medical device
Σ (n)	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
	Target
	Interval
	Legal Manufacturer

Symbol	Symbol Title and Description
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
	Printed with soy ink
	CE Mark
	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year month day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
MC DEF	Master Curve Definition
LOT DTL	Lot Details
UNITS C	Common Units
UNITS SI	International System of Units
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

US Pats 9,575,062; 6,664,043; 8,778,624; 7,309,615; 7,785,904.

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