SIEMENS

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

SARS-CoV-2 Total (COV2T)

For Use Under Emergency Use Authorization Only

For *in vitro* diagnostic use.

For prescription use only.

Assay for the Detection of Total Antibodies to SARS-CoV-2

Current Revision and Date[a]	Rev. 01, 2020-05	
Product Name	ADVIA Centaur SARS-CoV-2 Total (COV2T)	REF 11206710 (100 tests) REF 11206922 (500 tests)
Abbreviated Product Name	ADVIA Centaur COV2T	
Test Name/ID	COV2T	
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur COV2T QC	REF 11206713
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199 (112351)
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Specimen Types	Serum, potassium EDTA plasma, lithium heparin plasma	
Sample Volume	50 µL	
Measuring Interval	0.05–10.00 Index	

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

Intended Use

The ADVIA Centaur® SARS-CoV-2 Total (COV2T) assay is a chemiluminescent immunoassay intended for qualitative detection of total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum and plasma (potassium EDTA and lithium heparin) using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. The ADVIA Centaur SARS-CoV-2 Total (COV2T) assay is intended as an aid in identifying patients with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, to perform moderate or high complexity tests.

Results are for the detection of SARS CoV-2 antibodies. Antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

The sensitivity of the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay early after infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The ADVIA Centaur SARS-CoV-2 Total (COV2T) assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation

COVID-19 (coronavirus disease 2019) is the illness resulting from infection with SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) virus.[1-5] The virus spreads readily from person to person or possibly from environmental exposure.[6] Evidence supports spread by both asymptomatic and symptomatic individuals.[7] About 20% of infections identified to date produce severe disease, principally Acute Respiratory Distress Syndrome (ARDS), requiring intensive care unit treatment.[4,8,9] Differentiating COVID-19 from other respiratory pathogens is essential for implementing infection control measures, such as isolation and contact tracing, as well as clinical monitoring and support.

Diagnosis of current infection with SARS-CoV-2 relies primarily on molecular testing for the viral RNA using a swab collection for sputum or throat/nasal secretions.[10,11] SARS-CoV-2 RNA testing is recommended as the most sensitive diagnostic test for early infection, as viral RNA can be detected prior to antibody seroconversion.[12,13] Production of antibodies to the virus (such as IgM and IgG) occur within 15 days in most patients, and seroconversion can be coincident with the continued detection of viral RNA.[13-16]

Serology testing is essential for disease surveillance. This is particularly true for understanding viral prevalence, as most infections cause mild or no symptoms. Assessment of antibodies to SARS-CoV-2 virus in the population aids in the understanding of disease spread (both current and recovered) and may support the assessment of immunity should the presence of antibodies prove to be protective.

Principles of the Procedure

The ADVIA Centaur COV2T assay is a fully automated 1-step antigen sandwich immunoassay using acridinium ester chemiluminescent technology, in which antigens are bridged by antibodies present in the patient sample. The Solid Phase contains a preformed complex of streptavidin-coated microparticles and biotinylated SARS-CoV-2 recombinant antigens. This reagent is used to capture anti-SARS-CoV-2 antibodies in the patient sample. The Lite Reagent contains acridinium-ester-labeled SARS-CoV-2 recombinant antigens used to detect anti-SARS-CoV-2 antibodies bound to the Solid Phase.

A direct relationship exists between the amount of SARS-CoV-2 antibodies present in the patient sample and the amount of relative light units (RLUs) detected by the system.

A result of reactive or nonreactive is determined according to the Index Value established with the calibrators. Refer to *Interpretation of Results*.

Reagents

Material Description	Storage	Stability
ADVIA Centaur COV2T ReadyPack® primary reagent pack[a, b] **Lite Reagent** 10.0 mL/reagent pack Recombinant SARS-CoV-2 S1 RBD antigen (~0.3 µg/mL) labeled with acridinium ester in buffer; bovine serum albumin; goat serum; surfactant; sodium azide (< 0.1%) **Solid Phase** 10.0 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated SARS-CoV-2 S1 RBD antigen (~1.0 µg/mL) in buffer; bovine serum albumin; goat serum; surfactant; sodium azide (< 0.1%)	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
ADVIA Centaur COV2T CAL[a, b] 1.0 mL/vial Processed* human plasma negative for antibodies to SARS-CoV-2 and processed* human plasma spiked with antibodies to SARS-CoV-2; sodium azide (< 0.1%) **Processed plasma is defibrinated and filtered plasma.*	Unopened at 2–8°C Opened at 2–8°C At room temperature	Until expiration date on product 60 days 8 hours
ADVIA Centaur Wash 1[a, c] 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, c] 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 *Materials Required but Not Provided*.

Warnings and Precautions

For Use Under Emergency Use Authorization Only

For *in vitro* diagnostic use only.

For prescription use only.

This test has not been FDA cleared or approved; the test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, to perform moderate or high complexity tests.

This test has been authorized only for detecting the presence of antibodies against SARS-CoV-2, not for any other viruses or pathogens.

This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

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.

CAUTION POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[17-19]

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.

Storage and Stability

Store all reagents at 2–8°C 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 (potassium EDTA and lithium heparin) are the recommended sample types for this assay. Do not use heat-inactivated specimens.

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.[18]

- Keep tubes capped at all times.[18]
- Test specimens as soon as possible after collecting. Store specimens at 2–8°C if not tested immediately within 8 hours.

Storing the Specimen

- Thawed frozen specimens must be clarified by centrifugation prior to testing. Do not store in a frost-free freezer.
- Freeze samples, devoid of red blood cells, at ≤ -20°C for longer storage.

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.

Store samples capped and upright at 2–8°C upon arrival. If shipment is expected to exceed 2 days, 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.[18]

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11206710	1 ReadyPack primary reagent pack containing ADVIA Centaur COV2T Lite Reagent and Solid Phase 1 vial ADVIA Centaur COV2T CAL low calibrator CAL L 1 vial ADVIA Centaur COV2T CAL high calibrator CAL H ADVIA Centaur COV2T master curve card ADVIA Centaur COV2T CAL calibrator assigned value sheets and barcode labels	100
11206922	5 ReadyPack primary reagent packs containing ADVIA Centaur COV2T Lite Reagent and Solid Phase 2 vials ADVIA Centaur COV2T CAL low calibrator CAL L 2 vials ADVIA Centaur COV2T CAL high calibrator CAL H ADVIA Centaur COV2T master curve card ADVIA Centaur COV2T CAL calibrator assigned value sheets and barcode labels	500

Materials Required but Not Provided

The following materials are required to perform these assays, but are not provided:

REF	Description	
	ADVIA Centaur XP System[a] ADVIA Centaur XPT System[a]	
11206713	ADVIA Centaur COV2T QC (quality control material)	2 x 2.0 mL negative quality control, level 1 CONTROL − 1 2 x 2.0 mL positive quality control, level 2 CONTROL + 2 Quality control assigned value sheet and barcode labels
01137199 (112351)	ADVIA Centaur Wash 1 (wash)	2 x 1500 mL/pack WASH 1
03773025	ADVIA Centaur Wash 1 (wash)	2 x 2500 mL/pack 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.

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Solid Phase, then incubates for 3 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. After mixing the packs, load the packs into the reagent holders in the primary reagent compartment, starting from left to right.

Preparing the System

A daily cleaning procedure must be completed prior to and after your laboratory's batched testing for the ADVIA Centaur COV2T assay.

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* 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 COV2T assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

Calibration Frequency

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

- At the end of the 14-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.

Preparing the Calibrators

Calibrators are liquid and ready to use. Allow the calibrators to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material.

Use calibrators within the stability limits specified in *Reagents* and discard any remaining material.

Calibration Procedure

The calibrators are provided in dropper vials. Each dispensed drop is approximately 50 µL.

Perform the calibration procedure for each assay using the following steps:

1. Ensure that the appropriate master curve and calibrator assigned values are entered on the system. For information about defining the master curve and entering calibrator values, refer to the system online help.
2. Load the required reagents for the assay.
3. Schedule the calibrators.

4. Label two sample containers with barcode labels: one container for the low calibrator and one container for the high calibrator. Place the barcode labels on the sample containers with the readable characters oriented vertically.

   Note Barcode labels are lot-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

5. Gently mix the product and dispense a sufficient volume of each calibrator into the appropriate sample containers. Avoid bubbles.

   The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help.

6. Load the samples according to the system online help.

Note Dispose of any calibrator that remains in the sample container after 8 hours. Do not refill or reuse sample containers. Do not return any calibrator material back into the original container.

Performing Quality Control

For quality control of the ADVIA Centaur COV2T assay, use the ADVIA Centaur COV2T QC 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.

A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system or within your interval, as determined by an appropriate 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.

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

Test quality control samples after a successful calibration.

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. Refer to *Interpretation of Results*.

Interpretation of Results

The system reports ADVIA Centaur COV2T assay results in Index Values and as Nonreactive or Reactive:

- **Nonreactive:** < 1.0 Index. These samples are considered negative for SARS-CoV-2 antibodies.
- **Reactive:** ≥ 1.0 Index. These samples are considered positive for SARS-CoV-2 antibodies.

The cut-off value for the ADVIA Centaur COV2T assay was verified based on clinical agreement 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:

- This assay should not be used to diagnose or exclude acute infection. Results are not intended to be used as the sole basis for patient management decisions. Test results should be interpreted in conjunction with clinical observations, patient history, epidemiological information, and other laboratory findings.
- The performance of the assay has not been established with cord blood, neonatal specimens, cadaver specimens, or body fluids other than serum or plasma.
- A reactive test result does not exclude past or present infection by other coronaviruses, such as SARS-CoV-1, MERS-CoV, HKU1, 229E, NL63, or OC43.
- Patient specimens may be nonreactive if collected during the early (pre-seroconversion) phase of illness or due to a decline in titer over time. In addition, the immune response may be depressed in elderly, immunocompromised, or immunosuppressed patients.
- It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to re-infection.
- This test should not be used for donor screening.

Conditions of Authorization for the Laboratory

The ADVIA Centaur SARS-CoV-2 Total (COV2T) assay Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website:

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd

However, to assist clinical laboratories using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay, the relevant Conditions of Authorization are listed below:

- Authorized laboratories[a] using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay will include with result reports of the assay, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay will use the product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay are not permitted.
- Authorized laboratories that receive the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay will notify the relevant public health authorities of their intent to run the assay prior to initiating testing.
- Authorized laboratories using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories will collect information on the performance of the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay and report to DMD/OHT7-OIR/OPEQ/ CDRH (via email: CDRH EUA Reporting@fda.hhs.gov) and Siemens Healthineers Technical Support (https://www.siemens-healthineers.com/en-us/ or tel: 1-877-229-3711) any suspected occurrence of false reactive or false non reactive results and significant deviations from the established performance characteristics of the assay of which they become aware.

- All laboratory personnel using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay.
- Siemens Healthineers, authorized distributors, and authorized laboratories using the ADVIA Centaur SARS-CoV-2 Total (COV2T) assay will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

[a] The letter of authorization refers to, "Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate or high complexity tests" as "authorized laboratories".

Performance Characteristics

Measuring Interval

0.05–10.00 Index is reported as nonreactive (< 1.0 Index) or reactive (≥ 1.0 Index).

Clinical Agreement

Positive percent agreement and negative percent agreement were determined in accordance with CLSI Document EP12-A2.[22] A retrospective study was conducted in order to evaluate the clinical performance of the ADVIA Centaur COV2T assay. The performance of the ADVIA Centaur COV2T assay was determined by testing a total of 1851 samples using the ADVIA Centaur XP system.

Positive Percent Agreement

Positive percent agreement was determined by testing 262 samples collected over the course of time from 67 unique donor subjects with a clinical diagnosis of COVID-19 based on a positive polymerase chain reaction (PCR) method. The following table describes positive percent agreement by time of sampling following a positive PCR result:

Days Post PCR Positive	Number Tested	Reactive	Nonreactive	Positive Percent Agreement (95% CI)
0–6	95	58	37	61.05% (50.50%–70.89%)
7–13	120	117	3	97.50% (92.87% –99.48%)
≥14	47	47	0	100.00% (92.45% –100.00%)

Negative Percent Agreement

Negative percent agreement was determined by testing 1589 samples collected prior to the COVID-19 outbreak (before November 2019) from apparently healthy individuals and apparently healthy pregnant women in the United States. The results are shown in the table below:

Group	Number Tested	Nonreactive	Reactive	Negative Percent Agreement (95% CI)
Apparently Healthy	1489	1486	3	99.80% (99.41%–99.96%)
Apparently Healthy Pregnant Women	100	100	0	100.00% (96.38%–100.00%)
Total	**1589**	**1586**	**3**	**99.81% (99.45%–99.96%)**

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[23] A single-site precision study for the ADVIA Centaur COV2T assay was conducted. Samples and assay controls (a Negative Control and a Positive Control) were assayed in duplicate in 2 runs per day for 5 days using the ADVIA Centaur XP system. Results for the precision of the ADVIA Centaur COV2T assay are presented in the following table:

			Repeatability		Within-Laboratory Precision	
Specimen Type	N[a]	Mean (Index)	SD[b] (Index)	CV[c] (%)	SD (Index)	CV (%)
Serum A	20	0.74	0.069	9.3	0.092	12.4
Serum B	20	1.31	0.034	2.6	0.068	5.2
Control 1	20	0.04	0.034	N/A[d]	0.046	N/A
Control 2	20	1.10	0.119	10.8	0.119	10.8

[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	
Index Value	**Repeatability (Within-Run)**	**Within-Laboratory (Total Precision)**
0.70–2.00	≤ 12.0% CV	≤ 15.0% CV

Results obtained at individual laboratories may vary from the data presented.

Specimen Equivalency

Matched sample sets (serum, EDTA plasma, and lithium heparin plasma) from the same donors were used for the matrix comparison studies. Negative samples for each claimed specimen type/matrix were spiked with the same amount of analyte (SARS-CoV-2 antibody positive patient sample) in order to have negative (unspiked), high negative, and low positive analyte levels. Specimen equivalency was determined by testing the samples with the ADVIA Centaur COV2T assay using the ADVIA Centaur XP system. Using a Deming linear regression model, results from plasma samples were compared to serum results in accordance with CLSI Document EP09-A3.[24] The following results were obtained:

Tube (y) vs. Serum (x)	N[a]	Sample Interval	Slope	Intercept	r[b]
EDTA (plasma)	18	0.08–1.92	0.98	0.03	0.979
lithium heparin (plasma)	18	0.08–2.04	0.99	0.05	0.979

[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 EP07-ed3.[25] The impact of potentially interfering substances on the detection of SARS-CoV-2 antibodies with the ADVIA Centaur COV2T assay was evaluated with endogenous substances commonly found in serum and plasma specimens, including biotin, conjugated bilirubin, unconjugated bilirubin, hemoglobin, and triglycerides. Serum samples were spiked with SARS-CoV-2 antibody at the following levels: unspiked, high negative (~0.6 Index), and low positive (~1.0 Index). Results were established using the Atellica IM COV2T assay, which has the same reagent formulations as the ADVIA Centaur COV2T assay. Testing demonstrated a ≤ 10% change for each substance at the indicated concentration.

Substance	Substance Test Concentration
Hemoglobin	1000 mg/dL
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Triglycerides (Intralipid)	2000 mg/dL
Biotin	3500 ng/mL

Cross-Reactivity

Cross-reactivity was determined in accordance with CLSI Document EP07-ed3.[25] The assay was evaluated for potential cross-reactivity using specimens containing antibodies to other pathogens and other disease states using the ADVIA Centaur COV2T assay with the ADVIA Centaur XP system. No false positive results were observed with the potential cross-reactants listed in the following table:

Clinical Category	Number Tested	Number Reactive with ADVIA Centaur COV2T Assay
Anti nuclear antibody (ANA)	5	0
Chlamydia IgG	5	0
Cytomegalovirus (CMV) IgG	5	0
Epstein Barr virus (EBV) IgG	5	0
Epstein Barr virus (EBV) IgM	5	0
Graves' disease	5	0
Hepatitis A virus (HAV) IgM	5	0
Hepatitis B core (anti-HBc) IgM	5	0
Hepatitis C virus (HCV) antibody	5	0
Human anti-mouse antibody (HAMA)	5	0
Human herpes virus (HHV) IgM	3	0
Human immunodeficiency virus (HIV) antibody	10	0
Influenza antibody	10	0
Measles antibody	5	0
Parvovirus B19 antibody	5	0
Rheumatoid factor (RF)	5	0
Varicella zoster virus (VZV) antibody	5	0
Total	**93**	**0**

Results obtained at individual laboratories may vary from the data presented.

Standardization

The ADVIA Centaur COV2T assay standardization is traceable to an internal standard based on agreement with known positive and negative SARS-CoV-2 samples.

Currently no reference standard is available for this assay.

Technical Assistance

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

siemens-healthineers.com

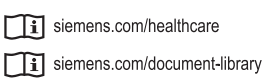
References

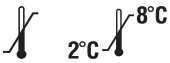
1. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents*. 2020;55(3):105924.
2. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, *et al*. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Mil Med Res*. 2020;7(1):11.
3. Li H, Liu SM, Yu XH, Tang SL, Tang CK. Coronavirus disease 2019 (COVID-19): current status and future perspectives. *Int J Antimicrob Agents*. 2020;29:105951.
4. Wu Z and McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323(13):2648.
5. Pan A, Liu L, Wang C, Guo H, Hao X, Wang Q, *et al*. Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. *JAMA*. 2020:6130.
6. Rothan HA and Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun*. 2020;109:102433.
7. Lai CC, Liu YH, Wang CY, Wang YH, Hsueh SC, Yen MY, *et al*. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths. *J Microbiol Immunol Infect*. 2020;pii: S1684-1182;(20):30040-2.
8. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, *et al*. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*. 2020;10:1001.
9. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, *et al*. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;13:101623.
10. Centers for Disease Control and Prevention (CDC). Coronoavirus Disease 2019: Evaluation and Testing page. https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Accessed April 27, 2020
11. World Health Organization. Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans page. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance. Accessed April 27, 2020
12. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, *et al*. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (COVID-19) infected pneumonia (standard version). *Mil Med Res*. 2020;7(1):4.
13. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, *et al*. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020;pii:344.
14. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, *et al*. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020;10.1002:25727.
15. Yang JR, Deng DT, Wu N, Yang B, Li HJ, and Pan XB. Persistent viral RNA positivity during recovery period of a patient with SARS-CoV-2 infection. *J Med Virol*. 2020:10.10002:25940.
16. Wu F, Wang A, Liu M, Wang Q, Chen J, Xia S, *et al*. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv; https://doi.org/10.1101/2020.03.30.20047365. Accessed April 30, 2020.

17. Centers for Disease Control. Perspectives in disease prevention and health promotion update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR*. 1988;37(24):377–382, 387–388.
18. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
19. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M29-A4.
20. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007. CLSI Document GP41-A6.
21. Clinical and Laboratory Standards Institute. *Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP39-A6.
22. Clinical and Laboratory Standards Institute. *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2008. CLSI Document EP12-A2.
23. Clinical and Laboratory Standards Institute. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document EP05-A3.
24. Clinical and Laboratory Standards Institute. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI Document EP09-A3.
25. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. CLSI Document EP07-ed3.

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
Rev. REVISION	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.

Symbol	Symbol Title and Description
	Corrosive
	Dangerous to environment
	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.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner
	*In vitro* diagnostic medical device
	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.

Symbol	Symbol Title and Description
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.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
	Authorized Representative in the European Community
	Use-by date Use by the designated date.
	Batch code
	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)
	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
	Master Curve Definition
	Lot Details
	Common Units
	International System of Units
	Material

Symbol	Symbol Title and Description
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens-healthineers.com

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

Siemens Healthcare Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens-healthineers.com

Global Division
Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens-healthineers.com

SIEMENS

ADVIA Centaur®
Immunoassay Systems

SARS-CoV-2 Total Quality Control (COV2T QC)

Current Revision and Date[a]	Rev. 01, 2020-05
Product Name	ADVIA Centaur SARS-CoV-2 Total Quality Control (COV2T QC)
Abbreviated Product Name	ADVIA Centaur COV2T QC
	2 x 2.0 mL negative quality control, level 1 CONTROL – 1 REF 11206713 2 x 2.0 mL positive quality control, level 2 CONTROL + 2 Quality control assigned value sheet and barcode labels
Systems	ADVIA Centaur systems

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

FOR USA:

For Use Under Emergency Use Authorization Only

For *in vitro* diagnostic use.

For Professional Use.

CE

Intended Use

The ADVIA Centaur® SARS-CoV-2 Total Quality Control (COV2T QC) is for *in vitro* diagnostic use in monitoring the precision and accuracy of the ADVIA Centaur® SARS-CoV-2 Total (COV2T) assay using the ADVIA Centaur® systems.

Material Description

Material Description	Storage	Stability
ADVIA Centaur COV2T QC 2.0 mL/vial Processed human plasma nonreactive and reactive for SARS-CoV-2 antibodies; sodium azide (< 0.1%)	At 2–8°C	Until expiration date on product
	Opened at 2–8°C	60 days
	At room temperature	8 hours

Warnings and Precautions

FOR USA:

For Use Under Emergency Use Authorization Only

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.

CAUTION POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[1-3]

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.

Storage and Stability

Store quality control materials in an upright position. Quality control materials are stable until the expiration date on the product when stored at 2–8°C. 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 storage and stability, refer to *Material Description*.

Performing Quality Control

Perform the quality control procedure at least once during each day that samples are analyzed. Test quality control samples after a successful calibration.

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

Treat all quality control samples the same as patient samples.

Preparing the Quality Control Materials

Quality control materials are liquid and ready to use. Gently mix and invert the vials to ensure homogeneity of the material.

Note Use quality control material within the stability limits specified in *Material Description* and discard any remaining material.

Quality Control Procedure

The quality control material is provided in dropper vials. Each dispensed drop is approximately 50 µL.

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help. Perform the quality control procedure using the following steps:

1. Ensure that the quality control definitions are defined, and that the quality control values are entered on the system using the assigned value sheet provided.
2. Ensure that the required reagents are loaded for the assay.
3. Schedule the quality control samples to the worklist.
4. Label two sample containers with barcode labels: one sample container for the positive control, and one sample container for the negative control.

   Note Barcode labels are lot-specific. Do not use barcode labels from one lot of controls with any other lot of controls.
5. Gently mix each vial of quality control material and dispense at least 5-6 drops into the appropriate sample container. Avoid bubbles.

   Note This procedure uses sufficient volumes to test each product in duplicate.
6. Load the samples according to the system online help.

Note Dispose of any QC material that remains in the sample container after 8 hours. Do not refill or reuse sample containers. Do not return any QC material back into the original container.

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 system online help.

Expected Values

For the assigned values, refer to the quality control assigned value sheet provided. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system or within your interval, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering QC definitions, refer to the system online help.

The assigned values are traceable to the standardization of the assay. For additional information, refer to the assay instructions for use.

Limitations

The ADVIA Centaur COV2T QC is for use only with the ADVIA Centaur COV2T assay. Assay values have not been established for assays other than the ADVIA Centaur COV2T assay.

The results obtained using quality control material depend on several factors. Erroneous results can occur from causes such as improper storage, inadequate mixing, reconstitution errors, or sample handling errors associated with system or assay procedures.

The assigned control values should be used as a guide in evaluating performance. The control targets and intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the established interval. Each laboratory should establish corrective measures if individual values fall outside the interval. Follow the applicable government regulations and local guidelines for quality control.

Technical Assistance

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

siemens-healthineers.com

References

1. Centers for Disease Control. Perspectives in disease prevention and health promotion update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR*. 1988;37(24):377–382, 387–388.
2. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
3. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M29-A4.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF	Catalog number
	Legal Manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE XXXX	CE Mark with notified body ID number Notified body ID number can vary.
	Consult instructions for use		Biological risks Potential biological risks are associated with the medical device.
	Do not freeze		Temperature limit
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight Prevent exposure to sunlight and heat.		Up Store in an upright position.
	Use-by date Use by the designated date.	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.
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision

Symbol	Definition	Symbol	Definition
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	PRINTED WITH SOY INK	Printed with soy ink
	Recycle	**RxOnly**	Prescription device (US only)

Legal Information

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens-healthineers.com

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

Siemens Healthcare Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens-healthineers.com

Global Division
Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens-healthineers.com