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ADVIA® 1800
ADVIA® 2400
Chemistry Systems

Calcium (CA)

Current Revision and Date[a]	Rev. G, 2020-02	
Product Name	ADVIA® Chemistry Calcium (CA) Reagents	REF 04802312 (6 × 675 tests per kit) REF 07506552 (7 × 358 tests per kit)
Systems	ADVIA 1800 Chemistry System ADVIA 2400 Chemistry System	
Materials Required but Not Provided	Siemens Chemistry Calibrator Reagent container adapters Commercially available controls	REF 09784096 (T03-1291-62)
Specimen Types	Human serum, plasma (lithium heparin), urine	
Assay Principle	*o*-cresolphthalein complexone (CPC)	
Assay Range	Serum: 1.0–15.0 mg/dL (0.25–3.75 mmol/L) Plasma: 1.0–15.0 mg/dL (0.25–3.75 mmol/L) Urine: 1.0–30.0 mg/dL (0.25–7.50 mmol/L)	
Reagent Storage	15–25°C	
Reagent On-System Stability	14 days when you are not using a reagent container insert 30 days when you are using a reagent container insert	
Reagent Code	74061	

[a] In Rev. F or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

For *in vitro* diagnostic use in the quantitative determination of calcium in human serum, plasma (lithium heparin), or urine on ADVIA® Chemistry systems. Such measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal failure, and tetany.

Summary and Explanation

The ADVIA Chemistry Calcium (CA) assay is based on the work of Gitelman (*o*-cresolphthalein complexone without deproteinization).[1]

Principles of the Procedure

Calcium ions form a violet complex with *o*-cresolphthalein complexone in an alkaline medium. The reaction is measured at 545/658 nm.

Reaction Equation

$$CPC + 2\ Ca^{2+} \longrightarrow CPC\ (Ca^{2+})_2\ Complex$$

Reagents

Reagent	Description	Storage	Reagent Stability
REF 04802312	**ADVIA Chemistry Calcium (CA) Reagents**		
Calcium Reagent 1 CA R1	68 mL in 70-mL containers Ethanolamine buffer (1.0 mol/L) NaN_3 (0.02%)	15–25°C	**Unopened:** Stable until the expiration date on product. **On-system:** • 14 days when you are not using a reagent container insert • 30 days when you are using a reagent container insert
Calcium Reagent 2 CA R2	33.5 mL in 40-mL containers *o*-Cresolphthalein complexone (0.338 mmol/L) 8-Hydroxyquinoline (13.78 mmol/L)	15–25°C	**Unopened:** Stable until the expiration date on product. **On-system:** • 14 days when you are not using a reagent container insert • 30 days when you are using a reagent container insert
REF 07506552	**ADVIA Chemistry Calcium (CA) Reagents**		
Calcium Reagent 1 CA R1	38 mL in 40-mL containers Ethanolamine buffer (1.0 mol/L) NaN_3 (0.02%)	15–25°C	**Unopened:** Stable until the expiration date on product. **On-system:** • 14 days when you are not using a reagent container insert • 30 days when you are using a reagent container insert
Calcium Reagent 2 CA R2	17.3 mL in 20-mL containers *o*-Cresolphthalein complexone (0.338 mmol/L) 8-Hydroxyquinoline (13.78 mmol/L)	15–25°C	**Unopened:** Stable until the expiration date on product. **On-system:** • 14 days when you are not using a reagent container insert • 30 days when you are using a reagent container insert

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

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 the buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H314, H335 **P280, P310, P304+P340, P301+P330+P331, P303+P361+P353, P305+P351+P338, P501**	**Danger!** Causes severe skin burns and eye damage. May cause respiratory irritation. Wear protective gloves/protective clothing/eye protection/face protection. Immediately call a POISON CENTER or doctor/physician. IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. IF SWALLOWED: rinse mouth. Do NOT induce vomiting. IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** 2-aminoethanol; ADVIA Chemistry Calcium Reagent 1

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.

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

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Before use, gently invert the capped reagent to disrupt bubbles and ensure homogeneity. If bubbles still exist or foam is present, use a clean transfer pipette to aspirate them from the reagent container prior to use.

Storing and Stability

Unopened reagents are stable until the expiration date printed on the product label when stored at 15–25°C. Do not freeze reagents.

Specimen Collection and Handling

Note Do not use sodium oxalate, EDTA, or sodium fluoride as anticoagulants, as they have been found to interfere.

Siemens Healthcare Diagnostics validated serum, plasma (lithium heparin), and urine for the ADVIA Chemistry CA assay.

Follow these guidelines for specimens used for this assay:

- Serum and plasma can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[2] Follow the instructions provided with your specimen collection device for use and processing.[3]
- Complete clot formation should take place before centrifugation.
- Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of 2 hours from the time of collection.[4]
- Specimens should be free of particulate matter.
- Specimens should be as fresh as possible.

The purpose of handling and storage information is to provide guidance to users. 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.

Procedure

Materials Provided

The following materials are provided:

Item	Contents	Number of Tests
REF 04802312	Reagent 1: 6 × 70-mL container Reagent 2: 6 × 40-mL container	6 × 675
REF 07506552	Reagent 1: 7 × 40-mL container Reagent 2: 7 × 20-mL container	7 × 358

Materials Required but Not Provided

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

Item	Description
REF 09784096 (T03-1291-62)	Siemens Chemistry Calibrator
REF 02404085	20-mL reagent container adapter for 40-mL slot (ADVIA 1800)
REF 05249323	20-mL reagent container adapter for 70-mL slot (ADVIA 1800)
REF 00771668	20-mL reagent container adapter for 70-mL slot (ADVIA 2400)
REF 08163594	40-mL reagent container adapter for 70-mL slot (ADVIA 2400)
	Commercially available control materials

Optional Materials

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

Item	Description
REF 02991886	Reagent container insert

Assay Procedure

Sampling, reagent delivery, mixing, and processing are automatically performed by the ADVIA Chemistry system.

For detailed information on performing the procedure, refer to the system operating instructions.

Preparing the System

For detailed information on preparing the system, refer to the system operating instructions.

Preparing the Samples

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Chemistry CA reagents are stable on the system for 14 days when you are not using a reagent container insert, and for 30 days when you are using a reagent container insert.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry CA assay, use the Siemens Chemistry Calibrator (REF 09784096 (T03-1291-62)).

Enter the lot-specific calibrator values that are provided with each lot of calibrator. Perform the calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay every day when you are not using a reagent container insert. Calibrate the assay every 4 days when you are using a reagent container insert.

Calibrate the assay after the following events:

- When the reagent lot number changes
- When a reagent pack is replaced by a new reagent pack with the same lot number, and the previous reagent pack was recalibrated during use
- When a reagent pack is replaced by a new reagent pack with the same lot number, and an additional reagent blank was run on the previous reagent pack during use
- After replacing critical optical or hydraulic components
- When indicated by quality control procedures

Individual laboratory quality control programs and procedures may require more frequent calibration.

Reagent Blank (RBL) Frequency

The ADVIA Chemistry system measures the RBL during assay calibration.

Note Use deionized water as the sample for the RBL in the ADVIA Chemistry CA assay.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

At least once each day of use, analyze 2 levels (low and high) of a commercially available quality control (QC) material with known calcium concentrations.

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

The actual frequency of control in a laboratory is based on many factors, such as workflow, system experience, and government regulation. Each laboratory should evaluate the controls based on the frequency established by their laboratory guidelines.

Also, assay controls under the following conditions:

- Whenever you use a new reagent lot
- Following any system maintenance, cleaning, or troubleshooting procedure
- After performing a new calibration or an additional reagent blank

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Taking Corrective Action

If the quality control results do not fall within the expected control range or within the laboratory's established values, do not report results. Take the following actions:

1. Determine and correct the cause of the unacceptable control results:
   a. Verify that the assay was performed according to the instructions for use.
   b. Verify that the materials are not expired.
   c. Verify that required maintenance was performed.
   d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
   e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat the prior step.
   f. If necessary, contact your local technical support provider or distributor for assistance.
2. After corrective action is complete, repeat required testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

The system calculates and reports results based on the absorbance measurements of the test sample during the test, and of the calibrator(s) from calibration.

The instrument calculates the concentration of calcium in mg/dL (common units) or mmol/L (SI units).

Conversion factor: mg/dL × 0.25 = mmol/L

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

A number of substances cause physiological changes in serum, plasma, or urine analyte concentrations. A comprehensive discussion of possible interfering substances, their serum, plasma, or urine concentrations, and their possible physiological involvements is beyond the scope of this document. Consult the listed reference for specific details on known potential interfering substances.[5]

As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.

Siemens has determined that there is a possibility for certain ADVIA Chemistry reagents to interact with the ADVIA Chemistry CA assay when run on the same system. To mitigate these carryover events, the ADVIA Chemistry system software provides a Contamination Avoidance process. For further information and instructions to establish this process on your systems, refer to the Customer Bulletin entitled: *Consolidated Directory of Contamination Avoidance Settings for ADVIA Chemistry XPT Systems* (PN 10815606, latest revision).

Expected Values

The reference range for calcium is listed in the following table.

Sample Type	Reference Range
Serum/Plasma[6]	8.3–10.6 mg/dL (2.08–2.65 mmol/L)
Urine[7]	100–300 mg/day (2.5–7.5 mmol/day)

Siemens provides this information for reference. As with all *in vitro* diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results. Consider these values as a guideline only.

Performance Characteristics

Analytical Measuring Range

This assay is linear from 1.0–15.0 mg/dL (0.25–3.75 mmol/L) for serum and plasma, and 1.0–30.0 mg/dL (0.25–7.50 mmol/L) for urine.

Results that are below the assay range are flagged **L**. You should report the test result as < 1.0 mg/dL (< 0.25 mmol/L) for serum and plasma, and < 1.0 mg/dL (< 0.25 mmol/L) for urine.

Results that are above the assay range are flagged **H**.

Extended Measuring Range

Siemens has validated an automatic rerun condition for this assay that extends the reportable range to 30.0 mg/dL (7.50 mmol/L) for serum and plasma.

You may configure the system to trigger automatic reruns. Rerun results will be flagged **R**.

Precision

The precision of the ADVIA Chemistry CA assay was evaluated according to the CLSI protocol EP05-A2.[8] Each sample was assayed 2 times per run, 1 or 2 runs per day, for at least 20 days.

ADVIA 1650/1800

		Repeatability (Within-Run)		Within-Lab (Total)	
Specimen Type	**Mean**	**SD[a]**	**CV[b] (%)**	**SD**	**CV (%)**
Common Units (mg/dL)					
Control 1	19.0	0.21	1.1	0.76	4.0
Control 2	35.5	0.58	1.6	1.78	5.0
Control 3	51.7	1.50	2.9	2.66	5.1
SI Units (g/L)					
Control 1	0.19	0.002	1.1	0.008	4.0
Control 2	0.36	0.006	1.6	0.018	5.0
Control 3	0.52	0.015	2.9	0.027	5.1

[a] SD = standard deviation

[b] CV = coefficient of variation

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		Repeatability (Within-Run)		Within-Lab (Total)	
Specimen Type	**Mean**	**SD[a]**	**CV[b] (%)**	**SD**	**CV (%)**
Common Units (mg/dL)					
Serum	5.9	0.04	0.7	0.16	2.7
Serum	10.8	0.10	0.9	0.32	2.9
Serum	12.0	0.07	0.6	0.42	3.5
Urine	6.2	0.05	0.8	0.15	2.4
Urine	21.2	0.12	0.5	0.52	2.5
SI Units (mmol/L)					
Serum	1.48	0.01	0.7	0.04	2.7
Serum	2.70	0.02	0.9	0.08	2.9
Serum	3.00	0.02	0.6	0.10	3.5
Urine	1.55	0.01	0.8	0.04	2.4
Urine	5.30	0.03	0.5	0.13	2.5

[a] SD = standard deviation
[b] CV = coefficient of variation

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		Repeatability (Within-Run)		Within-Lab (Total)	
Specimen Type	**Mean**	**SD[a]**	**CV[b] (%)**	**SD**	**CV (%)**
Common Units (mg/dL)					
Serum	6.2	0.06	1.0	0.12	2.0
Serum	8.5	0.17	2.0	0.21	2.4
Serum	10.9	0.18	1.6	0.23	2.1
Urine	5.8	0.10	1.7	0.12	2.1
Urine	12.7	0.08	0.6	0.64	5.1
SI Units (mmol/L)					
Serum	1.55	0.02	1.0	0.03	2.0
Serum	2.13	0.04	2.0	0.05	2.4
Serum	2.73	0.04	1.6	0.06	2.1

		Repeatability (Within-Run)		Within-Lab (Total)	
Specimen Type	**Mean**	**SD[a]**	**CV[b] (%)**	**SD**	**CV (%)**
Urine	1.45	0.03	1.7	0.03	2.1
Urine	3.18	0.02	0.6	0.16	5.1

[a] SD = standard deviation

[b] CV = coefficient of variation

Actual results will vary depending on the study design, and on the sample and sample population used. Results obtained at individual laboratories may vary from the data provided.

Accuracy / Method Comparison

The performance of the ADVIA Chemistry CA assay (y) was compared with the performance of the comparison assay on the indicated system (x).

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Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sy.x	Sample Range
Serum	Technicon DAX®	100	y = 0.99x + 0.13	0.22	0.971	7.0–13.2 mg/dL
			y = 0.99x + 0.03	0.06	0.971	1.8–3.3 mmol/L
Plasma[a]	ADVIA 1650 (serum)	59	y = 0.94x + 0.82	0.09	0.963	9.0–10.8 mg/dL
			y = 0.94x + 0.21	0.02	0.963	2.3–2.7 mmol/L
Urine	Dimension	32	y = 1.20x - 2.25	0.17	0.999	3.7–14.5 mg/dL
			y = 1.20x - 0.56	0.04	0.999	0.9–3.6 mmol/L
Urine	Beckman CX3	63	y = 1.07x + 0.03	0.56	0.988	2.1–14.7 mg/dL
			y = 1.07x + 0.01	0.14	0.988	0.5–3.7 mmol/L
Serum	Reference Method	48	y = 0.98x - 0.49	0.26	0.997	2.5–13.9 mg/dL
			y = 0.98x - 0.12	0.07	0.997	0.6–3.5 mmol/L

[a] lithium heparin

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Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sy.x	Sample Range
Serum	ADVIA 1650	242	y = 1.01x + 0.27	0.17	0.988	4.6–12.1 mg/dL
			y = 1.01x + 0.07	0.04	0.988	1.2–3.0 mmol/L
Urine	ADVIA 1650	64	y = 0.98x + 0.23	0.14	0.999	1.0–15.0 mg/dL
			y = 0.98x + 0.06	0.04	0.999	0.3–3.8 mmol/L
Serum	Reference Method	48	y = 1.00x - 0.56	0.29	0.996	2.5–13.9 mg/dL
			y = 1.00x - 0.14	0.07	0.996	0.6–3.5 mmol/L

The correlation of the assay may vary depending on the study design, comparable method, and sample population. Results obtained at individual laboratories may vary from the data provided.

Interferences

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Interferent	Interferent Level	Calcium Sample Concentration	Interference
Bilirubin	30 mg/dL (513 µmol/L)	7.6 mg/dL (1.90 mmol/L)	NSI[a]
Hemolysis (hemoglobin)	525 mg/dL (5.25 g/L)	7.6 mg/dL (1.90 mmol/L)	NSI
Lipemia[b] (from Intralipid)	650 mg/dL (7.35 mmol/L)	7.6 mg/dL (1.90 mmol/L)	NSI

[a] NSI = No significant interference. A percentage effect ≥ 10% is considered a significant interference.

[b] SI units calculated as triolein

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Interferent	Interferent Level	Calcium Sample Concentration	Interference
Bilirubin	30 mg/dL (513 µmol/L)	6.3 mg/dL (1.57 mmol/L)	NSI[a]
Hemolysis (hemoglobin)	525 mg/dL (5.25 g/L)	6.3 mg/dL (1.57 mmol/L)	NSI
Lipemia[b] (from Intralipid)	625 mg/dL (7.06 mmol/L)	7.1 mg/dL (1.77 mmol/L)	NSI

[a] NSI = No significant interference. A percentage effect ≥ 10% is considered a significant interference.

[b] SI units calculated as triolein

Note There is poor correlation between turbidity and triglyceride concentration in a lipemic sample.[9]

Actual results will vary depending on the study design, the levels of the potential interferences tested, and the samples used. Results obtained at individual laboratories may vary from the data provided.

Standardization

The ADVIA Chemistry CA assay is traceable to a National Institute of Standards and Technology (NIST) atomic absorption reference method, which uses reference materials from NIST via patient sample correlation. Refer to the correlation data in the *Accuracy/Method Comparison* section for the relationship. Assigned values of the Siemens Chemistry Calibrator are traceable to this standardization.

Technical Assistance

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

siemens.com/healthcare

References

1. Gitelman HJ. An improved procedure for the determination of calcium in biochemical specimens. *Ana Biochem.* 1967;18:521–531.
2. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Guideline—Sixth Edition.* CLSI document GP41-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
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4. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline—Fourth Edition.* CLSI document GP44-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
5. Young DS. *Effects of Drugs on Clinical Laboratory Tests.* 5th ed. Washington, DC: AACC Press; 2000.
6. Data on file at Siemens Healthcare Diagnostics.
7. Wu AHB, ed. *Tietz Clinical Guide to Laboratory Tests*, 4th ed. St. Louis, MO: WB Saunders Company; 2006:204.
8. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* CLSI document EP05-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004.
9. Twomey PJ, Don-Wauchope AC, McCullough D. Unreliability of triglyceride measurement to predict turbidity induced interference. *J Clin Pathol.* 2003 Nov;56(11):861–862.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Keep away from sunlight and heat		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Do not freeze (> 0°C)		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
Rev.	Revision	YYYY-MM-DD	Date format (year-month-day)
LOT	Batch code	**RxOnly**	Prescription Device (US only)

Trademarks

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