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ADVIA Centaur® CP
Immunoassay Systems

Active-B12 (Holotranscobalamin) (AB12)

Current Revision and Date[a]	Rev. C, 2022-05	
Product Name	ADVIA Centaur® AB12 assay	REF 10995088
Systems	ADVIA Centaur CP system	
Materials Required but Not Provided	ADVIA Centaur Ancillary Probe Wash 3	REF 10699211
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Specimen Types	Human serum	
Measuring Interval	5.00–146.00 pmol/L	
Reagent Storage	2–8°C	
Reagent On-System Stability	38 days	

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

Intended Use

The ADVIA Centaur® Active-B12 (Holotranscobalamin) (AB12) assay is for *in vitro* diagnostic use in the quantitative measurement of holotranscobalamin (holoTC) in human serum using the ADVIA Centaur CP system. Active-B12 (holotranscobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency.

Summary and Explanation

Vitamin B12 (cobalamin) in serum is bound to two proteins: transcobalamin and haptocorrin. The transcobalamin-vitamin B12 complex is called holotranscobalamin (holoTC). HoloTC contains the biologically available cobalamin as only holoTC promotes the uptake of cobalamin by all cells via specific receptors. In comparison, approximately 80% of the circulating cobalamin, that is carried by haptocorrin, is considered metabolically inert because no cellular receptors exist, with the exception of receptors found in the liver.

Genetic absence of haptocorrin is rare and not considered a serious condition. Genetic absence or abnormalities of transcobalamin, however, manifest as typical hematological, neurological, and metabolic pathologies of cobalamin deficiency, which require aggressive treatment even if a serum analysis results in normal cobalamin concentrations.

The shorter circulating half-life of holoTC compared to holohaptocorrin (holoHC) makes a decrease of holoTC one of the earliest markers of cobalamin deficiency.[1]

The measurement of total serum cobalamin suffers from some limitations; in particular, most of the cobalamin that is measured is bound to haptocorrin. A number of studies have been published to support that holoTC is a better indicator of vitamin B12 status than total serum cobalamin.[2,3] Methods based on specific anti-transcobalamin antibodies have been available and confirm the usefulness of holoTC for diagnosing B12 deficiency.

As expected, holoTC levels are low in patients with biochemical signs of vitamin B12 deficiency.[4] Notably, low values have been reported in vegetarians,[5] vegans,[6] and in populations with low intake of vitamin B12.[7] HoloTC levels reflect vitamin B12 status, independent of recent absorption of the vitamin.[8]

Principles of the Procedure

The ADVIA Centaur AB12 assay is a fully automated, two-step direct immunoassay using chemiluminescent technology. The assay utilizes an acridinium ester-labeled anti-transcobalamin antibody as the Lite Reagent. The Solid Phase consists of biotinylated anti-holotranscobalamin antibody coupled to streptavidin-coated magnetic latex microparticles.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur AB12 ReadyPack® primary reagent pack; Lite Reagent	5.0 mL/reagent pack anti-transcobalamin (TC) monoclonal antibody 3-11 (0.5 µg/mL) labeled with acridinium ester in buffer with surfactant, bovine serum albumin, and sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on product **On-system:** 38 days
ADVIA Centaur AB12 ReadyPack primary reagent pack; Solid Phase Reagent	15.0 mL/reagent pack streptavidin coated paramagnetic microparticles preformed with biotinylated anti-holoTC monoclonal antibody 3C4 (~0.4 mg/mL) in buffer, bovine serum albumin, surfactant, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on product **On-system:** 38 days
ADVIA Centaur AB12 Calibrator	2.0 mL/vial recombinant holotranscobalamin, bovine serum albumin and sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on product
		2–8°C	**Opened:** 30 days **On-system:** 8 hours
ADVIA Centaur Wash 1[a] WASH 1	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on product **On-system:** 1 month
ADVIA Centaur Wash 1[a] WASH 1	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on product **On-system:** 1 month

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 13[b] M-DIL 13	10 mL/pack buffer with surfactant and sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on product **On-system:** 28 consecutive days after the pack is pierced
ADVIA Centaur ReadyPack ancillary reagent pack; Ancillary Probe Wash 3[a] APW 3	25.0 mL/reagent pack phosphate-buffered saline with sodium azide (< 0.1%), surfactant	2–8°C	**Unopened:** Stable until the expiration date on pack **On-system:** 1 month

[a] *See Materials required but Not Provided.*
[b] *See Optional Materials.*

Warnings and Precautions

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

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.

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

For professional use.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use. Remove all of the reagents from the refrigerator, and mix all primary reagent packs by hand. Visually inspect the bottom of the reagent packs to ensure that all particles are dispersed and resuspended before loading them onto the system. For detailed information about preparing the reagents for use, refer to the system operating instructions.

Note

- Discard reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store ADVIA Centaur AB12 reagent packs upright at 2–8°C away from heat and light sources. Reagent packs loaded on the system are protected from light. Reagents are stable at 2–8°C until the expiration date on the product.

Store ADVIA Centaur AB12 Calibrators at 2–8°C. Calibrators are stable at 2–8°C until the expiration date on the product.

Do not use ADVIA Centaur materials beyond the expiration date printed on the product.

For onboard stability, refer to *On-System Stability*.

Specimen Collection and Handling

This assay has been validated for use with human serum samples. The handling and storage information provided here has been validated.

Collecting the Specimen

- Collect all blood samples observing universal precautions for venipuncture.
- Handle all specimens as if capable of transmitting disease.
- Serum can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[9]
- Follow the instructions provided with your specimen collection device for use and processing.[10]
- Complete clot formation should take place before centrifugation.[11]
- Centrifuge specimens as soon as possible with a maximum limit of two hours from the time of collection.
- Keep tubes stoppered at all times.[11]
- Do not use specimens with apparent contamination.

Storing the Specimen

- Separated specimens are stable for 16 hours at room temperature, 3 days at 2–8°C. For longer storage, specimens may be frozen for 3 months at -20°C or colder. Avoid more than 1 freeze/thaw cycle. Do not store in a frost-free freezer.
- Thoroughly mix all thawed samples and centrifuge before testing.

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 alternative 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 specimens stoppered at 2–8°C upon arrival.
- If shipment is expected to exceed 2 days, ship specimens frozen.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10995088	1 ReadyPack primary reagent pack containing ADVIA Centaur AB12 Lite Reagent and Solid Phase	100
	1 vial ADVIA Centaur AB12 low calibrator CAL L	
	1 vial ADVIA Centaur AB12 high calibrator CAL H	
	ADVIA Centaur systems AB12 Master Curve card	
	ADVIA Centaur systems AB12 Calibrator Assigned Value card	

Materials Required but Not Provided

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

Item	Description	
REF 10699211	ADVIA Centaur Ancillary Probe Wash 3 APW 3	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack
REF 01137199	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF 03773025	ADVIA Centaur Wash 1[a] WASH 1	2 x 2500 mL/pack

[a] For use with systems with 2500 mL capacity.

Optional Materials

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

Item	Description	
REF 10995091	ADVIA Centaur AB12 Quality Control	1 x 7.0 mL control 1 CONTROL 1
		1 x 7.0 mL control 2 CONTROL 2
	ADVIA Centaur systems AB12 lot-specific value sheet	
REF 10492364	ADVIA Centaur Multi-Diluent 13 M-DIL 13	2 ReadyPack ancillary reagent packs containing 10.0 mL/pack
REF 10995090	ADVIA Centaur AB12 Master Curve Material	5 x 2.0 mL
	ADVIA Centaur systems AB12 lot-specific value sheet	

Assay Procedure

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

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 150 µL of Solid Phase and incubates the mixture for 10 minutes at 37°C.
3. Separates the Solid Phase from the mixture, and aspirates the unbound reagent.
4. Washes the cuvettes, resuspends the particles in ADVIA Centaur Wash 1, and incubates for 4 minutes at 37°C.
5. Dispenses 50 µL of Lite Reagent into the cuvette and incubates for 18 minutes at 37°C.
6. Separates the Solid Phase from the mixture, and aspirates the unbound reagent.

7. Washes the cuvettes in ADVIA Centaur Wash 1.
8. Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
9. Calculates the results from the relative light units (RLU) generated using a stored master curve, and reports in pmol/L.

A direct relationship exists between the amount of active-B12 present in the patient sample and the amount of relative light units (RLUs) detected by the system.

The system washes the reagent probe with ADVIA Centaur Ancillary Probe Wash 3 to mitigate potential interference between the ADVIA Centaur AB12 assay and other assays.

Preparing the System

Ensure that the system has sufficient primary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Mix the primary reagents by hand. Refer to *Preparing Reagents*. Load the ReadyPack primary reagent packs in the primary reagent compartment. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

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 detailed information about determining the minimum required volume, refer to the system operating instructions.

Note The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. For detailed information, refer to *Dilutions*.

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

- Samples are free of fibrin or other particulate matter. Remove particulates by centrifugation.
- Samples are free of bubbles or foam.

On-System Stability

The ADVIA Centaur AB12 assay reagents are stable unopened until the expiration date on the product or onboard the system for 38 days. Discard reagent packs at the end of the 38-day on-system stability interval. Do not use reagents beyond the expiration date.

Reagent packs loaded on the system are protected from light.

The ADVIA Centaur AB12 calibrators are stable unopened until the expiration date on the product or onboard the system for 8 hours. For opened bottle stability, refer to *Reagents*.

Performing Calibration

For calibration of the ADVIA Centaur AB12 assay, use ADVIA Centaur AB12 Calibrators provided with each kit.

Note The low and high calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each lot of calibrators contains a lot-specific Calibrator Assigned Value card to facilitate entering the calibration values on the system. Enter the values using the barcode scanner or the keyboard. For detailed information about entering calibrator values, refer to the system operating instructions.

Performing the Calibration

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve values are entered on the system as needed, Refer to *Defining Master Curve Values*.
2. Ensure that the calibrator values are entered on the system.
3. Ensure that the required reagents are loaded for the assay.
4. Schedule the calibrators to the worklist.
5. Label 2 sample cups with calibrator barcode labels: 1 cup for the low calibrator and another cup for the high calibrator.

Note Place the barcode label on the sample cup with the readable characters oriented vertically.

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

6. Gently mix the low and high calibrators and dispense at least 5–6 drops into the appropriate sample cups. Avoid bubbles.

Note Each drop from the calibrator vial is approximately 50 µL.

Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.

7. Load the sample cups in a rack.
8. Place the rack in the sample compartment.
9. At the main menu, open the Reagent Compartment Screen.
10. Select the assay to calibrate.
11. Select **Calibrate.**

Note Dispose of any calibrator remaining in the sample cups after 8 hours. Do not return any calibrators back into the vials after calibration because evaporation can occur, which may affect performance. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Calibration Frequency

Calibrate the assay at the end of the 30-day calibration interval. Additionally, the ADVIA Centaur AB12 assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Defining Master Curve Values

The ADVIA Centaur AB12 assay requires you to enter Master Curve values when using a new reagent lot number. For each new lot number of Lite Reagent and Solid Phase, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

To monitor system performance and chart trends, as a minimum requirement, assay two levels of quality control material that contain active-B12, on each day that samples are analyzed. Test quality control samples when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Siemens Healthcare Diagnostics recommends the use of ADVIA Centaur Active-B12 Quality Control (REF 10995091) or an equivalent commercially available control material with at least two levels. A satisfactory level of performance is achieved when the analyte values obtained are within the acceptable control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

Perform the quality control procedure according to the quality control instructions for use.

For detailed information about how to enter quality control values, refer to the system operating instructions.

Refer to the lot-specific value sheet for the suggested target values and ranges specific for the lot number of the controls.

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 suggested target values and ranges or within the laboratory's established values, do not report results.

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instruction for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports active-B12 results in pmol/L (SI units).

The ADVIA Centaur Active-B12 assay results can be converted to pg/mL (common units).

The conversion factor is (pmol/L x 43) = pg/mL.

The system will display results below the Limit of Quantitation of 5.00 pmol/L. These results are considered below the sensitivity of the assay and should be reported as < 5.00 pmol/L.

Dilutions

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:2	100

The following information pertains to dilutions:

- Results below the measuring interval are reported as < 5.00 pmol/L and results above the measuring interval (> 146.00 pmol/L) require dilution to obtain a reportable result.
- Patient samples can be automatically diluted by the system. Use ADVIA Centaur Multi-Diluent 13 (REF 10492364) to dilute patient samples.
- For automatic dilutions, ensure that the ADVIA Centaur Multi-Diluent 13 is loaded. Set the system parameters as follows:

  Dilution Point: ≤ 146.00 pmol/L

  Dilution factor: 2

  For detailed information about automatic dilutions, refer to the system operating instructions.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Do not use ADVIA Centaur AB12 test results interchangeably with test results from other active-B12 assays.

Sample results are invalid and must be repeated if the controls are out of range.

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

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur AB12 assay is limited to the detection of the active-B12 in human serum.
- The performance of the ADVIA Centaur AB12 assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum, such as saliva, urine, amniotic, or pleural fluids.
- The performance of the assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Heterophilic antibodies in human serum can react with the immunoglobulins included in the assay components causing interference with *in vitro* immunoassays.[12] Samples from patients routinely exposed to animals or animal serum products can demonstrate this type of interference, which can potentially cause an anomalous result. Additional information may be required for diagnosis.
- Potential interferences from monoclonal gammopathies were not investigated.

Expected Values

The ADVIA Centaur AB12 assay results were obtained on 123 apparently healthy males (n = 73) and females (n = 50) using the ADVIA Centaur XP system. Subjects were not pre-screened for the consumption of dietary supplements, including vitamin B12. The age range was 21–69 years. The mean active-B12 concentration for the group was established at 90.24 pmol/L with a 95% central reference interval from 27.24–169.62 pmol/L according to EP28-A3c.[13]

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results. Consider these values as guidelines only.

Performance Characteristics on the ADVIA Centaur XP System

The results included in this section were obtained from testing using the ADVIA Centaur XP system.

Measuring Interval

The ADVIA Centaur AB12 assay measures active-B12 concentrations from 5.00–146.00 pmol/L.

Specificity

The ADVIA Centaur AB12 assay shows minimal cross-reactivity with other B12 binding proteins, apotranscobalamin and haptocorrin.

Cross-reactivity was tested in the presence of active-B12 (concentrations of approximately 30 pmol/L and 70 pmol/L) according to CLSI EP07-A2[14] using the ADVIA Centaur AB12 assay.

Percent cross-reactivity is calculated as:

$$\% \text{ cross-reactivity} = \frac{(\text{concentration of spiked sample} - \text{concentration of unspiked sample})}{\text{concentration of cross-reactant}} \times 100$$

The following results were obtained:

Cross-reactant	Concentration (pmol/L)	Cross-reactivity (%)
Apotranscobalamin	250	0.2
	500	-0.1
Haptocorrin	2500	-0.4
	5000	-0.4

Interferences

Potential interference in the ADVIA Centaur AB12 assay from hemoglobin, bilirubin, and triglyceride, is designed to have a bias of $\leq$ 10% at active-B12 concentrations of 28.14–37.23 pmol/L and 69.78–76.66 pmol/L.

Interfering substances at the levels indicated in the table below were tested as described in CLSI Document EP07-A2[14] using the ADVIA Centaur AB12 assay.

Serum specimens that are...	Have an insignificant effect on the assay up to...
hemolyzed	500 mg/dL (0.31 mmol/L) of hemoglobin
icteric	60 mg/dL (1026 µmol/L) of unconjugated bilirubin
icteric	40 mg/dL (475 µmol/L) of conjugated bilirubin
lipemic	1000 mg/dL of triglyceride

Two levels of active-B12 were tested with each of the following substances at the levels indicated, and caused no significant interference in the ADVIA Centaur AB12 assay at active-B12 concentrations of 28.14–37.23 pmol/L and 69.78–76.66 pmol/L.

Substances	Concentrations
Biotin	1,000,000 ng/mL (4,093,300 nmol/L)
Cholesterol	500 mg/dL (12.95 mmol/L)
Human IgG	12 g/dL (120 g/L)
Methotrexate	91 mg/dL (2.00 mmol/L)
Perimethamine	75 µg/mL (302 µmol/L)
Rheumatoid Factor	200 IU/mL
Silwet L720	0.2 mg/dL
Total Proteins	12 g/dL (120 g/L)

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

Dilution Recovery

Eight samples containing high levels of active-B12 (87.50–223.17 pmol/L) were diluted 1:2 (1 part sample plus 1 part diluent) with ADVIA Centaur Multi-Diluent 13 and assayed for recovery correcting the diluted sample by the dilution factor.

In a representative study the observed percent recovery for individual samples ranged from 71%–122%.

$$\% \text{ Recovery} = \frac{\text{Observed dilution dose}}{\text{Expected dilution dose}} \times 100$$

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

Performance Characteristics on the ADVIA Centaur CP System

The results included in this section were obtained from testing using the ADVIA Centaur CP system.

Detection Capability

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined as described in CLSI Document EP17-A2.[15] The ADVIA Centaur AB12 assay was designed to have an LoQ of $\leq$ 5.00 pmol/L.

The LoB is defined as the highest measurement result that is likely to be observed for a blank sample.

The LoD is defined as the lowest concentration of active-B12 that can be detected with 95% probability. The ADVIA Centaur AB12 assay has an LoD of 2.99 pmol/L based on 240 determinations using 8 low level samples, and an LoB of 2.73 pmol/L.

The LoQ is defined as the lowest concentration of active-B12 that can be detected at a within-laboratory CV of 8%. The ADVIA Centaur AB12 assay has an LoQ of 5.00 pmol/L.

Report results below the LoQ as < 5.00 pmol/L.

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

Precision

Precision was evaluated according to the CLSI protocol EP05-A3.[16] The assay precision was designed to have Within-Laboratory %CV less than or equal to 7.0% for levels less than or equal to 30.00 pmol/L and less than or equal to 6.0% for levels greater than 30.00 pmol/L.

Four pooled serum samples were prepared with active-B12 concentrations spanning the measuring interval. Samples were tested in replicates of 2, in 2 runs per day over 20 days, yielding 80 observations per sample. One ADVIA Centaur CP system and 3 reagent lots were used. Representative data from the study is shown in the following table.

			Repeatability (Within-Run)		Within-Lab (Total)	
Specimen Type	n	Mean (pmol/L)	SD (pmol/L)	CV (%)	SD (pmol/L)	CV (%)
Sample 1	80	21.86	0.70	3.2	0.96	4.4
Sample 2	80	35.38	0.79	2.2	1.53	4.3
Sample 3	80	79.86	2.60	3.3	3.29	4.1
Sample 4	80	129.54	3.51	2.7	5.03	3.9

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

Method Comparison

The ADVIA Centaur AB12 assay using the ADVIA Centaur CP system is designed to have a correlation coefficient (r) $\geq$ 0.95 compared to using the ADVIA Centaur XP system.

A total of 113 human serum samples with active-B12 concentration in the range of 5.83–138.26 pmol/L were tested. The relationship of the ADVIA Centaur AB12 assay using the ADVIA Centaur CP system (y), and the ADVIA Centaur AB12 assay using the ADVIA Centaur XP system (x) is described using Passing-Bablok regression and a Pearson coefficient. Representative data from the study is shown below:

ADVIA Centaur AB12 (y) = 0.95 (x) + 0.24 pmol/L (intercept), r = 0.99.

The correlation of the assay may vary depending on the study design, comparable method, and sample population according to EP09-A3.[17] Assay results obtained at individual laboratories may vary from the data presented.

Specimen Collection Comparison

The ADVIA Centaur AB12 assay was evaluated using different serum matrices. The assay is designed to have a correlation coefficient (r) ≥ 0.95, a slope of 0.90–1.10, and an intercept $\pm$ 3.0 pmol/L for alternative tube types (y) versus serum (x).

A specimen collection study was performed with serum active-B12 values ranging from 8.70–136.96 pmol/L. Passing-Bablok regression and a Pearson coefficient analysis were performed and no significant difference between tube types was observed. The following results were obtained:

			Intercept	
Serum (x) vs	n	Slope	(pmol/L)	r
Serum Separator Tube (y)	57	1.00	0.45	1.00

Linearity

Linearity was evaluated according to the CLSI protocol EP06-A.[18] Two samples containing high levels of active-B12 were mixed with a pool of artificial serum matrix. The resulting sample mixtures were assayed for active-B12. The ADVIA Centaur AB12 assay is linear from 5.00–146.00 pmol/L.

High-Dose Hook Effect

Patient samples with high active-B12 levels can cause a paradoxical decrease in the relative light units (RLUs) (high-dose hook effect). In testing of the ADVIA Centaur AB12 assay using the ADVIA Centaur CP system, patient samples with active-B12 levels as high as 2089.29 pmol/L will assay greater than 146.00 pmol/L.

Standardization

The ADVIA Centaur AB12 assay is traceable to World Health Organization (WHO) International Standard for holotranscobalamin (HoloTC); NIBSC code 03/178. Assigned values for calibrators are traceable to this standard. The relationship of the ADVIA Centaur AB12 assay (y) to the WHO NIBSC 03/178 reference standard (x) was determined by dilution recovery on the ADVIA Centaur XP system (observed range of 9.78–101.76 pmol/L) and is described using a weighted linear regression and a Pearson coefficient.

Representative data from the study is shown below:

ADVIA Centaur AB12 (y) = 0.90 (x) - 0.12 pmol/L, r = 1.00.

Technical Assistance

For customer support, please contact your local technical support provider or distributor. siemens.com/healthcare.

References

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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 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
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
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	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
RxOnly	Prescription use only		

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