SIEMENS Healthineers

# Active-B12 (Holotranscobalamin) (AB12)

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| **Current Revision and Date**[a] | Rev. 02, 2019-10 | |
| **Product Name** | Atellica IM Active-B12 (Holotranscobalamin) (AB12) | REF 10733001 |
| **Abbreviated Product Name** | Atellica IM AB12 | |
| **Test Name/ID** | AB12 | |
| **Systems** | Atellica IM Analyzer | |
| **Materials Required but Not Provided** | Atellica IM APW1 | REF 10995458 |
| **Optional Materials** | Atellica IM AB12 QC | REF 10733002 |
| | Atellica IM Multi-Diluent 13 | REF 10995643 |
| | Atellica IM AB12 MCM | REF 10733003 |
| **Specimen Types** | Serum | |
| **Sample Volume** | 50 µL | |
| **Measuring Interval** | 4.25–146.00 pmol/L | |

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

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## Intended Use

The Atellica® IM Active-B12 (Holotranscobalamin) (AB12) assay is for *in vitro* diagnostic use in the quantitative measurement of holotranscobalamin (holoTC) in human serum using the Atellica® IM Analyzer. 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 Atellica IM AB12 assay is a fully automated, 2-step sandwich immunoassay using direct 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 paramagnetic microparticles.

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.

## Reagents

| Material Description | Storage | Stability[a] |
|---|---|---|
| **Atellica IM AB12 ReadyPack® primary reagent pack**<br>**Lite Reagent**<br>5.0 mL/reagent pack<br>Anti-transcobalamin (TC) monoclonal antibody 3-11 (0.5 µg/mL) labeled with acridinium ester; buffer; surfactant; bovine serum albumin (BSA); sodium azide (< 0.1%)<br>**Solid Phase**<br>15.0 mL/reagent pack<br>Streptavidin coated paramagnetic microparticles preformed with biotinylated anti-holoTC monoclonal antibody 3C4 (~0.4 mg/mL); buffer; BSA; surfactant; preservatives | Unopened at 2–8°C<br>Onboard | Until expiration date on product<br>28 days |
| **Atellica IM AB12 CAL**<br>2.0 mL/vial<br>Recombinant holotranscobalamin; BSA; sodium azide (< 0.1%) | Unopened at 2–8°C<br>Opened at 2–8°C<br>At room temperature<br>Atellica® Sample Handler[b] | Until expiration date on product<br>30 days after opening the product<br>8 hours |
| **Atellica IM Multi-Diluent 13 ReadyPack ancillary reagent pack[c]**<br>10 mL/pack<br>Buffer; surfactant; sodium azide (< 0.1%) | Unopened at 2–8°C<br>Onboard | Until expiration date on product<br>28 days |
| **Atellica IM APW1 ReadyPack ancillary reagent pack**<br>25.0 mL/pack<br>0.4 N sodium hydroxide | Unopened at 2–8°C<br>Onboard | Until expiration date on product<br>14 days |

[a] Refer to *Storage and Stability*.

[b] Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

[c] Refer to *Optional Materials*.

## Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

**CAUTION**

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

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

**CAUTION**

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

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|---|---|
| **H290,H319,H315** | **Warning!** |
| **P280,P264** | May be corrosive to metals. Causes serious eye irritation. Causes skin irritation. |
| **P305+P351+P338** | Wear protective gloves/protective clothing/eye protection/face protection. Wash |
| **P310,P390,P501** | hands thoroughly after handling. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations. |
| | **Contains:** sodium hydroxide (in Atellica IM APW1) |

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

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

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

**Note** For information about calibrator preparation, refer to *Preparing the Calibrators*.

## Storage and Stability

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

Store calibrators in an upright position. Unopened calibrators are stable until the expiration date on the product when stored at 2–8°C. Opened calibrators are stable for 30 days at 2–8°C or for 8 hours at room temperature.

Store Atellica IM Multi-Diluent 13 in an upright position. Unopened Atellica IM Multi-Diluent 13 is stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM APW1 in an upright position. Unopened Atellica IM APW1 is stable until the expiration date on the product when stored at 2–8°C.

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

## Onboard Stability

Reagents are stable onboard the system for 28 days. Discard reagents at the end of the onboard stability interval.

**Note** Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Atellica IM Multi-Diluent 13 is stable onboard the system for 28 days.

Atellica IM APW1 is stable onboard the system for 14 days.

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

# Specimen Collection and Handling

Serum is the recommended sample type for this assay.

## Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[9]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[10]
- Follow the instructions provided with your specimen collection device for use and processing.[11]
- Allow blood specimens to clot completely before centrifugation.[12]
- Centrifuge specimens as soon as possible with a maximum limit of 2 hours form the time of collection.
- Keep tubes capped at all times.[12]
- Test samples as soon as possible after collecting.

## Storing the Specimen

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

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 specimens stoppered at 2–8°C upon arrival.

If shipment is expected to exceed 2 days, ship specimens frozen.

## Preparing the Samples

Use plastic sample cups. Do not use glass sample cups for the Atellica IM AB12 assay. Use of glass sample cups will decrease recovery of the result.

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

If automatic dilution of a sample is required, load Atellica IM Multi-Diluent 13 in the reagent compartment. The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to *Dilutions*.

**Note** Do not use specimens with apparent contamination.

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

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

**Note** Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[12]

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

# Procedure

## Materials Provided

The following materials are provided:

| REF | Contents | Number of Tests |
|---|---|---|
| 10733001 | 1 ReadyPack primary reagent pack containing Atellica IM AB12 Lite Reagent and Solid Phase | 100 |
| | Atellica IM AB12 master curve and test definition MC TDEF | |
| | 1 vial Atellica IM AB12 CAL low calibrator CAL L | |
| | 1 vial Atellica IM AB12 CAL high calibrator CAL H | |
| | Atellica IM AB12 CAL lot-specific value sheet CAL LOT VAL | |

## Materials Required but Not Provided

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

| REF | Description | |
|---|---|---|
| | Atellica IM Analyzer[a] | |
| 10995458 | Atellica IM APW1 (probe wash) | 2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH |

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

## Optional Materials

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

| REF | Description | |
|---|---|---|
| 10733002 | Atellica IM AB12 QC (quality control material) | 1 x 7.0 mL quality control, level 1 CONTROL 1<br>1 x 7.0 mL quality control, level 2 CONTROL 2<br>Quality control lot-specific value sheet CONTROL LOT VAL |
| 10995643 | Atellica IM Multi-Diluent 13 (diluent) | 2 ReadyPack ancillary reagent packs containing 10.0 mL/pack DIL |
| 10733003 | Atellica IM AB12 MCM (master curve material) | 5 x 2.0 mL levels of master curve material MCM 1 - 5 |

## Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 150 µL of Solid Phase reagent, then incubates for 17 minutes at 37°C.
3. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
4. Resuspends the particles in Atellica IM Wash.
5. Dispenses 50 µL of Lite Reagent, then incubates the mixture for 17 minutes at 37°C.
6. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
7. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
8. Reports results.

**Note** The system will wash the reagent probe with Atellica IM APW1 to mitigate potential interference between assays.

## Preparing the Reagents

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

## Preparing the System

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

Ensure that Atellica IM APW1 is loaded in the reagent compartment.

For automated dilutions, ensure that Atellica IM Multi-Diluent 13 is loaded in the reagent compartment.

## Master Curve Definition

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

## Performing Calibration

For calibration of the Atellica IM AB12 assay, use the calibrators provided with each kit.

## Calibration Frequency

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

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

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

| Stability Interval | Days |
|---|---|
| Lot Calibration | 28 |
| Pack Calibration | 28 |
| Reagent Onboard Stability | 28 |

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

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

## Preparing the Calibrators

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

**Note** Use calibrators within the stability limits specified in *Storage and Stability* and discard any remaining material.

## Calibration Procedure

The calibrators are 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 online help.

Use plastic sample cups. Do not use glass sample cups for the Atellica IM AB12 CAL.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the lot-specific value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the online help.

## Performing Quality Control

For quality control of the Atellica IM AB12 assay, use the Atellica IM AB12 QC or an equivalent product at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

Use plastic sample cups. Do not use glass sample cups for the Atellica IM AB12 controls.

For the assigned values, refer to the lot-specific value sheet provided CONTROL | LOT | VAL. 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 quality control definitions, refer to the 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 assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

# Results

## Calculation of Results

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

Conversion formula: (pmol/L x 43) = pg/mL

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

## Dilutions

The measuring interval for serum is 4.25–146.00 pmol/L. For information about dilution options, refer to the online help.

Dilute and retest serum samples with active-B12 levels > 146.00 pmol/L to obtain reportable results.

For automated dilutions, ensure that Atellica IM Multi-Diluent 13 is loaded in the reagent compartment. Ensure that sufficient sample volume is available to perform the dilution and that the appropriate dilution factor is selected when scheduling the test, as indicated in the table below.

For automatic dilutions, enter a dilution setpoint ≤ 146.00 pmol/L.

| Sample | Dilution | Sample Volume (µL) |
|---|---|---|
| Serum | 1:2 | 100 |

## Interpretation of Results

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

**Note** If the controls are out of range, the sample results are invalid. Do not report results.

# Limitations

The following information pertains to limitations of the assay:

- The performance of the 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 fluid, or pleural fluid.
- The performance of the assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Potential interferences from monoclonal gammopathies were not investigated.
- Results obtained with the Atellica IM AB12 assay may not be used interchangeably with values obtained with different manufacturers' active-B12 methods.
- Use plastic sample cups. Do not use glass sample cups for the Atellica IM AB12 assay. Use of glass sample cups will decrease recovery of the results.
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[13,14] Additional information may be required for diagnosis.

# Expected Values

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

Results were obtained on 123 apparently healthy males (n = 73) and females (n = 50), who 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 CLSI Document EP28-A3c.[15]

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[15] Consider these values as guidance only.

# Performance Characteristics

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

## Measuring Interval

The Atellica IM AB12 assay provides results from 4.25–146.00 pmol/L. The lower end of the measuring interval is defined by the limit of quantitation (LoQ). Report results below the measuring interval as < 4.25 pmol/L.

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

## Specificity

Specificity was determined in accordance with CLSI Document EP07-A2.[16] The following substances were evaluated for cross-reactivity and do not interfere with the Atellica IM AB12 assay when present in serum at the concentrations indicated.

Cross reactivity was tested in the presence of active-B12 (concentrations of approximately 30 pmol/L and 70 pmol/L).

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:

| Substance | Substance Test Concentration (pmol/L) | Analyte Concentration (pmol/L) | Cross-reactivity (%) |
|---|---|---|---|
| Apotranscobalamin | 250 | 30 | 0.2 |
| | 250 | 70 | 0.1 |
| | 500 | 30 | -0.1 |
| | 500 | 70 | -0.1 |
| Haptocorrin | 2500 | 30 | -0.2 |
| | 2500 | 70 | -0.4 |
| | 5000 | 30 | -0.1 |
| | 5000 | 70 | -0.4 |

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

## Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[17] The assay is designed to have a limit of detection (LoD) ≤ LoQ, and an LoQ ≤ 5.00 pmol/L.

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

The limit of blank (LoB) corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoD corresponds to the lowest concentration of active-B12 that can be detected with a probability of 95%. The LoD for the Atellica IM AB12 assay is 0.83 pmol/L, and was determined using 160 determinations and an LoB of 0.46 pmol/L.

The LoQ corresponds to the lowest amount of active-B12 in a sample that can be detected at a within-laboratory CV of 8%. The LoQ of the Atellica IM AB12 assay is 4.25 pmol/L, and was determined using multiple patient samples in the interval 1.89–7.23 pmol/L. All samples were assayed in replicates of 8 in 1 run per day using 2 reagent lots, over a period of 5 days.

## Precision

Precision was determined in accordance with CLSI Document EP05-A3.[18] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days.

The assay was designed to have repeatability of ≤ 5% CV for samples ≥ 15.00 pmol/L.

The assay was designed to have within-laboratory precision of ≤ 7.0% CV for samples 15.00–30.00 pmol/L and ≤ 6.0% CV for samples > 30.00 pmol/L.

The following results were obtained:

| | | | Repeatability | | Within-Laboratory Precision | |
|---|---|---|---|---|---|---|
| **Specimen Type** | **N[a]** | **Mean (pmol/L)** | **SD[b] (pmol/L)** | **CV[c] (%)** | **SD (pmol/L)** | **CV (%)** |
| Serum A | 80 | 19.18 | 0.53 | 2.7 | 0.94 | 4.9 |
| Serum B | 80 | 32.69 | 0.87 | 2.7 | 1.24 | 3.8 |
| Serum C | 80 | 57.37 | 1.42 | 2.5 | 2.74 | 4.8 |
| Serum D | 80 | 77.82 | 2.00 | 2.6 | 3.33 | 4.3 |
| Serum E | 80 | 108.29 | 2.26 | 2.1 | 4.88 | 4.5 |

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.

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

## Assay Comparison

The Atellica IM AB12 assay is designed to have a correlation coefficient of (r) ≥ 0.95 and a slope of 1.0 ± 0.10 compared to the ADVIA Centaur AB12 assay. Assay comparison was determined using the Passing-Bablok regression model in accordance with CLSI Document EP09-A3.[19] The following results were obtained:

| **Specimen** | **Comparative Assay (x)** | **Regression Equation** | **Sample Interval** | **N[a]** | **r[b]** |
|---|---|---|---|---|---|
| Serum | ADVIA Centaur AB12 | y = 1.05x - 1.21pmol/L | 6.77–137.67 pmol/L | 113 | 0.98 |

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

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

## Specimen Equivalency

Specimen equivalency was determined using the Passing-Bablok regression model in accordance with CLSI Document EP09-A3.[19] The assay is designed to have a correlation coefficient (r) ≥ 0.95, and a slope of 0.90–1.10, intercept ± 3.0 pmol/L for alternate tube types versus serum. No significant difference was observed between tube types.

The following results were obtained:

| **Specimen (y)** | **Reference Specimen (x)** | **Regression Equation** | **Sample Interval** | **N[a]** | **r[b]** |
|---|---|---|---|---|---|
| Serum gel-barrier tube | Plain serum tube | y = 1.01x - 0.46 pmol/L | 24.00–143.44 pmol/L | 48 | 1.00 |

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

Agreement of the specimen types may vary depending on the study design and sample population used. Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

## Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2.[16]

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

The assay is designed to have ≤ 10% interference from hemoglobin, bilirubin, and lipemia at active-B12 concentrations of 28–37 pmol/L and 70–77 pmol/L. Interfering substances at the levels indicated in the table below were tested in accordance with CLSI Document EP07-A2.[16]

Bias is the difference in the results between the control sample (does not contain the interferent) and the test sample (contains the interferent) expressed in percent. Analyte results should not be corrected based on this bias.

| Substance | Substance Test Concentration Common Units (SI Units) | Analyte Concentration (pmol/L) | Bias (%) |
|---|---|---|---|
| Hemoglobin | 500 mg/dL (0.31 mmol/L) | 28–37<br>70–77 | -9.3<br>-7.4 |
| Bilirubin, conjugated | 40 mg/dL (475 µmol/L) | 28–37<br>70–77 | 5.0<br>4.5 |
| Bilirubin, unconjugated | 60 mg/dL (1026 µmol/L) | 28–37<br>70–77 | 3.3<br>-9.3 |
| Lipemia (Intralipid®)[a] | 1500 mg/dL (17 mmol/L) | 28–37<br>70–77 | -1.0<br>6.6 |

[a] Result was established using the Atellica IM analyzer.

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

The following substances do not interfere with the assay when present in serum at the concentrations indicated in the table below. Bias due to these substances is ≤ 10% at an analyte concentration of 28–37 pmol/L and 70–77 pmol/L.

| Substance | Substance Test Concentration Common Units (SI Units) | Analyte Concentration (pmol/L) | Bias (%) |
|---|---|---|---|
| Biotin | 1,000,000 ng/mL (4,093,300 nmol/L) | 28–37<br>70–77 | -5.4<br>5.2 |
| Cholesterol | 500 mg/dL (12.95 mmol/L) | 28–37<br>70–77 | 5.0<br>-2.5 |
| Human IgG | 12 g/dL (120 g/L) | 28–37<br>70–77 | -9.0<br>-9.4 |
| Methotrexate | 91 mg/dL (2.00 mmol/L) | 28–37<br>70–77 | 0.0<br>2.3 |
| Perimethamine | 75 µg/mL (302 µmol/L) | 28–37<br>70–77 | 1.0<br>-3.8 |
| Rheumatoid Factor | 200 IU/mL | 28–37<br>70–77 | -1.2<br>-6.1 |
| Total Proteins | 12 g/dL (120 g/L) | 28–37<br>70–77 | 5.9<br>2.2 |
| Triglycerides | 1000 mg/dL (11.3 mmol/L) | 28–37<br>70–77 | 2.8<br>0.1 |

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

## Dilution Recovery

Five samples containing high levels of active-B12 (147.33–166.26 pmol/L) were diluted 1:2 with Atellica IM Multi-Diluent 13 and assayed for recovery. The following results were obtained:

| Sample | Dilution | Observed (pmol/L) | Expected (pmol/L) | Recovery (%) |
|---|---|---|---|---|
| 1 | 1:2 | 122.52 | 147.33 | 83.2 |
| 2 | 1:2 | 114.31 | 160.56 | 71.2 |
| 3 | 1:2 | 133.34 | 166.26 | 80.2 |
| 4 | 1:2 | 119.40 | 151.04 | 79.1 |
| 5 | 1:2 | 125.55 | 153.35 | 81.9 |

Results were established using the Atellica IM Analyzer. Assay results obtained at individual laboratories may vary from the data presented.

## High-Dose Hook Effect

High active-B12 concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with active-B12 concentrations above the measuring interval and as high as 91,200 pmol/L will report > 146.00 pmol/L. Results were established using the Atellica IM Analyzer.

# Standardization

The Atellica IM 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. Results were established using the ADVIA Centaur system. The relationship of ADVIA Centaur AB12 assay (y) to the WHO NIBSC 03/178 reference standard (x) was determined by dilution recovery (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, contact your local technical support provider or distributor.

siemens.com/healthineers

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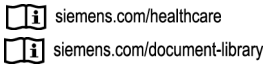
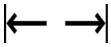
# Definition of Symbols

The following symbols may appear on the product labeling:

| Symbol | Symbol Title and Description |
|---|---|
|  | Consult instructions for use |
|   | Version of instructions for use |
|   | Internet URL address to access the electronic instructions for use |
|   | Revision |
|  | Caution<br>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<br>Potential biological risks are associated with the medical device. |
|  | Corrosive |
|  | Dangerous to environment |
|  | Irritant<br>Oral, dermal, or inhalation hazard |
|  | Inhalation hazard<br>Respiratory or internal health |
|  | Flammable<br>Flammable to extremely flammable |
|  | Oxidizing |
|  | Explosive |
|  | Toxic |
|  | Compressed gas |
|  | Keep away from sunlight<br>Prevent exposure to sunlight and heat. |
|  | Up<br>Store in an upright position. |

| Symbol | Symbol Title and Description |
|---|---|
|  | Do not freeze |
|  | Temperature limit<br>Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines. |
|  | Handheld barcode scanner |
| IVD | *In vitro* diagnostic medical device |
| Σ (n) | Contains sufficient for <n> tests<br>Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol. |
| **RxOnly** | Prescription device (US only)<br>Applies only to United States-registered IVD assays.<br>CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional. |
|  | Mixing of substances<br>Mix product before use. |
| g mL | Reconstitute and mix lyophilized product before use. |
|  | Target |
|  | Interval |
|  | Legal Manufacturer |
| EC REP | Authorized Representative in the European Community |
|  | Use-by date<br>Use by the designated date. |
| LOT | Batch code |
| REF | Catalog number |
|  | Recycle |
| PRINTED WITH SOY INK | Printed with soy ink |
| CE | CE Mark |
| CE 0088 | CE Mark with notified body ID number<br>Notified body ID number can vary. |
| **YYYY-MM-DD** | Date format (year month day) |
| CHECKSUM | Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid. |

| Symbol | Symbol Title and Description |
|---|---|
| UNITS C | Common Units |
| UNITS SI | International System of Units |
| MATERIAL | Material |
| MATERIAL ID | Unique material identification number |
| CONTROL NAME | Name of control |
| CONTROL TYPE | Type of control |

# Legal Information



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