This package insert must be read carefully prior to product use. Package insert instructions must be followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

- **REF** List Number
- **IVD** In Vitro Diagnostic Medical Device
- **℃** Store at 2-8°C
- **i** Consult instructions for use.
- **SN** Serial Number
- **REAGENT LOT** Reagent Lot
- **LOT** Lot Number
- **CONTROL NO.** Control Number
- **ASSAY CD-ROM** Assay CD-ROM
- **REACTION VESSELS** Reaction Vessels
- **SAMPLE CUPS** Sample Cups
- **SEPTUM** Septum
- **REPLACEMENT CAPS** Replacement Caps

See REAGENTS section for a full explanation of symbols used in reagent component naming.
It has been suggested that elevated homocysteine is a modifiable, independent risk factor for CAD, stroke and deep vein thrombosis. Studies have also identified elevated homocysteine as a strong independent risk factor for developing various forms of dementia, including Alzheimer’s Disease. In one study consisting of 1092 subjects from the Framingham Study, plasma homocysteine levels > 14 μmol/L doubled the risk of Alzheimer’s Disease.

A study has indicated plasma HCY levels are lower in pregnant women than non-pregnant women (mean HCY is approximately 5-8 μmol/L, values > 10 μmol/L are rarely observed). Increased HCY is associated with increased risk of pregnancy complications (preeclampsia, recurrent early pregnancy loss, premature delivery, low birth weight, and placental abruption or infarction). Maternal hyperhomocysteinemia is related to birth defects such as neural tube defects, orofacial clefts, club foot and Down’s Syndrome.

BIOLICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Homocysteine assay is a one-step immunoassay for the quantitative determination of total L-homocysteine in human serum or plasma using CMIA technology, with flexible assay protocols, referred to as Chemiflex. Bound or dimersed homocysteine (oxidized form) is reduced by diithiothreitol (DTT) to free homocysteine, which is then converted to S-adenosyl homocysteine (SAH) by the action of the recombinant enzyme S-adenosyl homocysteine hydrolase (rSAHHase) in the presence of excess adenosine. The SAH then competes with acridinium-labeled S-adenosyl cysteine for particle-bound monoclonal antibody. Following a wash stage and magnetic separation, pre-trigger and trigger solutions are added to the reaction mixture and the resulting chemiluminescence is measured as relative light units (RLUs). An indirect relationship exists between the amount of homocysteine in the sample and the RLUs detected by the ARCHITECT i10 System optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100 Tests

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT i10 Systems. Please contact your local distributor.

ARCHITECT Homocysteine Reagent Kit (1L71)

- **MICROPARTICLES**: 1 or 4 Bottle(s) (6.5 mL each) Anti-S-adenosyl-L-homocysteine (mouse, monoclonal) coated microparticles in Bis-Tris buffer with surfactants. Minimum concentration: 0.1% solids. Preservatives: sodium azide and other antimicrobial agents.
- **CONJUGATE**: 1 or 4 Bottle(s) (5.7 mL each) S-adenosyl-L-cysteine (SAC) acridinium-labeled conjugate in citrate buffer with surfactants. Minimum concentration: 1 mg/mL. Preservative: ProClin 300.
- **ENZYME**: 1 or 4 Bottle(s) (8.6 mL each) Recombinant S-adenosyl-L-homocysteine hydrolase (SAHase) in 4-(2-hydroxyethyl) piperezine-1-propanesulfonic acid (EPPS) buffer. Preservative: sodium azide.
- **REDUCTANT**: 1 or 4 Bottle(s) (21.5 mL each) Dithiothreitol (DTT) in citrate buffer.

Assay Diluent

ARCHITECT i10 Multi-Assay Manual Diluent (No. 7D82-50)

- **MULTI-ASSAY MANUAL DILUENT**: 1 Bottle (100 mL) ARCHITECT i10 Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents

ARCHITECT / Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION**: Pre-trigger solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT / Trigger Solution

- **TRIGGER SOLUTION**: Trigger solution containing 0.35 N sodium hydroxide.

ARCHITECT / Wash Buffer

- **WASH BUFFER**: Wash buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.
WARNINGS AND PRECAUTIONS

For In Vitro Diagnostic Use.

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens,18 Biosafety Level 220 or other appropriate biosafety practices21,22 should be used for materials that contain or are suspected of containing infectious agents.

The Conjugate contains methylisothiazolones, a component of ProClin, and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.

R43 May cause sensitization by skin contact.
S24 Avoid contact with skin.
S35 This material and its container must be disposed of in a safe way.
S37 Wear suitable gloves.
S46 If swallowed, seek medical advice immediately and show this container or label.

For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheets are available for professional user on request.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

Do not use reagent kits beyond the expiration date.

Do not pool reagents within a kit or between reagent kits.

Before loading the ARCHITECT Homocysteine Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the PROCEDURE, Assay Procedure section of this package insert.

Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.

To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.

• Once a septum has been placed on the reagent bottle, do not invert the bottle as this will result in reagent leakage and may compromise assay results.
• Over time, residual liquids may dry on the septum surface. These are typically dried salts, which have no effect on assay efficacy.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

The ARCHITECT Homocysteine Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.

When stored and handled as directed, reagents are stable until the expiration date.

The ARCHITECT Homocysteine Reagent Kit may be stored on board the ARCHITECT i System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. Recalibration may be required to obtain maximum onboard reagent stability. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

Reagents may be stored on or off the ARCHITECT i System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded. After reagents are removed from the system, initiate a reagent scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT Homocysteine assay file must be installed on the ARCHITECT i System from the ARCHITECT i Assay CD-ROM Addition F before performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

The default result unit for the ARCHITECT Homocysteine assay is μmol/L. An alternate result unit, μg/mL, may be selected for reporting results by editing assay parameter “Result concentration units” to μg/mL. The conversion factor used by the system is 0.1352.

• Concentration in μg/mL = Concentration in μmol/L x 0.1352

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT Homocysteine assay. Other specimen collection tubes have not been tested with this assay.

• Human serum and Serum Separator tubes
• Human plasma collected in:
  • lithium heparin
  • potassium EDTA
• Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
• The ARCHITECT i System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT Homocysteine assay.

Specimen Conditions

Do not use specimens with the following conditions:

• heat-inactivated
• grossly hemolyzed
• obvious microbial contamination
• cadaver specimens or any other body fluids
• For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
• Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
• For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
Preparation for Analysis

To minimize increases in homocysteine concentration from synthesis by red blood cells, place all specimens (serum and plasma) on ice after collection and prior to processing. Serum may clot more slowly and the volume of serum may be reduced as a result of being on ice.23

NOTE: Specimens not placed on ice immediately may exhibit a 10-20% increase in concentration.24

Follow the tube manufacturer’s processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.

Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.

To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged before testing if
- they contain fibrin, red blood cells, or other particulate matter,
- they require repeat testing, or
- they were frozen and thawed.

Transfer clarified specimen to a sample cup or secondary tube for testing.

Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

All specimens must be placed on ice immediately after collection. If testing will be delayed more than six hours,23 remove serum or plasma from the clot, red blood cells, or separator gel. Specimens may be stored for up to 14 days refrigerated at 2-8°C prior to being tested. If testing will be delayed more than 14 days, store frozen (≤ -20°C).

Serum or plasma specimens stored frozen for one year18 showed no performance difference. Avoid multiple freeze/thaw cycles.

Shipping

Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.

When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

Specimens may be shipped on wet or dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

1L71 ARCHITECT Homocysteine Reagent Kit

Materials Required but not Provided

ARCHITECT / System
1P38 ARCHITECT / ASSAY CD-ROM - WW (excluding US) - Addition F
1P39 ARCHITECT / ASSAY CD-ROM - US - Addition F
1L71-01 ARCHITECT Homocysteine Calibrators
1L71-10 ARCHITECT Homocysteine Controls
7D82-50 ARCHITECT / MULTI-ASSAY MANUAL DILUENT
ARCHITECT / PRE-TRIGGER SOLUTION
ARCHITECT / TRIGGER SOLUTION
ARCHITECT / WASH BUFFER
ARCHITECT / REACTION VESSELS
ARCHITECT / SAMPLE CUPS
ARCHITECT / SEPTUM
ARCHITECT / REPLACEMENT CAPS

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

Before loading the ARCHITECT Homocysteine Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.

- Invert the microparticle bottle 30 times.
- Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
- If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.

Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles refer to the Handling Precautions section of this package insert.

Load the ARCHITECT Homocysteine Reagent Kit on the ARCHITECT / System.

- Verify that all necessary assay reagents are present.
- Ensure that septums are present on all reagent bottles.

Order calibration, if necessary.

- For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.

Order tests.

- For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.

The minimum sample volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

- Priority: 78 μL for the first ARCHITECT Homocysteine test plus 28 μL for each additional ARCHITECT Homocysteine test from the same sample cup.
- ≤ 3 hours on board: 150 μL for the first ARCHITECT Homocysteine test plus 28 μL for each additional ARCHITECT Homocysteine test from the same sample cup.

If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.

Prepare Calibrators and Controls.

- ARCHITECT Homocysteine Calibrators and Controls should be prepared according to their respective package inserts.

To obtain the recommended volume requirements for the ARCHITECT Homocysteine Calibrators and Controls, hold the bottles vertically and dispense 5 drops of each calibrator or control into each respective sample cup.

Load samples.

- For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.

Press RUN.

- For additional information on principles of operation, refer to the ARCHITECT Operations Manual, Section 3.

For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with a homocysteine value exceeding 50.00 μmol/L are flagged with the code “>50.00” and may be diluted with the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Procedure

If using the Automated Dilution Protocol, the system performs a 1:10 dilution of the specimen and automatically calculates the concentrations of the specimen before dilution and reports the result.
**Manual Dilution Procedure**

- The suggested dilution for the ARCHITECT Homocysteine assay is 1:10.
- Add 20 μL of the patient specimen to 180 μL of the ARCHITECT / Multi-Assay Diluent (7D82-50).
- The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution. This will be the reported result.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

**Calibration**

- To perform an ARCHITECT Homocysteine calibration, test calibrators A, B, C, D, E, and F in replicates of two. A single sample of each homocysteine control must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- Calibration Range: 0.0 - 50.0 μmol/L.
- Once an ARCHITECT Homocysteine calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

**QUALITY CONTROL PROCEDURES**

The recommended control requirement for the ARCHITECT Homocysteine assay is that a single sample of each control be tested once every 24 hours each day of use. Laboratories should follow local, state and federal quality control procedures which may require more frequent use of controls to verify test results. The ARCHITECT Homocysteine Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

**Verification of Assay Claims**

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT Homocysteine assay belongs to method group 1. ARCHITECT Homocysteine Calibrators may be used in place of MasterCheck as described in the ARCHITECT System Operations Manual, Appendix B.

**RESULTS**

**Calculation**

The ARCHITECT Homocysteine assay uses a 4 Parameter Logistic Curve Fit (4PLC, Y-weighted) data reduction method to generate a calibration curve.

**Flags**

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

**Measurement Range (Reportable Range)**

The measurement range of the ARCHITECT Homocysteine assay is 1.00 μmol/L to 50.00 μmol/L.

**LIMITATIONS OF THE PROCEDURE**

- If the ARCHITECT Homocysteine assay results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- The following drugs may elevate levels of homocysteine: methotrexate, carbamazepine, phenytoin, nitrous oxide, anticonvulsants and 6-azauridine triacetate. The mechanism of action of these drugs affects different parts of the metabolic pathway of homocysteine.23,25
- S-adenosyl-methionine is an antidepressant whose molecular form is similar to S-adenosyl-homocysteine. This drug may interfere with the ARCHITECT Homocysteine assay.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).26,27 Specimens containing HAMA may produce anomalous values when tested with assay kits such as ARCHITECT Homocysteine that employ mouse monoclonal antibodies.28
- Heterophilic antibodies in human specimens can react with reagent immunoglobulins, interfering with in vitro immunoassays.29 Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert for specimen limitations.

### EXPECTED VALUES

Human EDTA plasma specimens from 300 apparently healthy individuals were evaluated using the ARCHITECT Homocysteine assay. The range of expected values is defined by the central 95% of the observations. The distribution is represented in the following table.*

<table>
<thead>
<tr>
<th>Sex</th>
<th>n</th>
<th>Median (μmol/L)</th>
<th>2.5% Percentile (μmol/L)</th>
<th>97.5% Percentile (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>150</td>
<td>9.05</td>
<td>5.46</td>
<td>18.20</td>
</tr>
<tr>
<td>Female</td>
<td>150</td>
<td>7.61</td>
<td>4.44</td>
<td>13.56</td>
</tr>
<tr>
<td>Overall</td>
<td>300</td>
<td>8.14</td>
<td>5.08</td>
<td>15.39</td>
</tr>
</tbody>
</table>

* Representative data; results in individual laboratories may vary from these data. It is recommended that each laboratory establish its own expected range, which may be unique to the population it serves depending upon geographical, patient, dietary, or environmental factors.

**SPECIFIC PERFORMANCE CHARACTERISTICS**

### Precision

The ARCHITECT Homocysteine assay is designed to have an assay precision of ≤ 10% total CV. A study was performed with guidance from the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Protocol EPS-A2.29 Three ARCHITECT Homocysteine Controls and five human plasma panels were assayed using two lots of reagents in replicates of two at two separate times per day for 20 days on two instruments. A new calibration curve was generated for each reagent lot on each day of testing. Data from this study are summarized in the following table.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>Instrument Lot</th>
<th>n</th>
<th>Mean (μmol/L)</th>
<th>Within Run SD</th>
<th>%CV</th>
<th>Total SD</th>
<th>%CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1</td>
<td>80</td>
<td>7.40</td>
<td>0.26</td>
<td>3.5</td>
<td>0.43</td>
<td>5.9</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>7.58</td>
<td>0.18</td>
<td>2.4</td>
<td>0.25</td>
<td>3.3</td>
</tr>
<tr>
<td>Medium</td>
<td>1</td>
<td>80</td>
<td>13.21</td>
<td>0.26</td>
<td>2.0</td>
<td>0.64</td>
<td>4.8</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>13.37</td>
<td>0.24</td>
<td>1.8</td>
<td>0.41</td>
<td>3.0</td>
</tr>
<tr>
<td>High</td>
<td>1</td>
<td>80</td>
<td>26.77</td>
<td>0.63</td>
<td>2.3</td>
<td>1.09</td>
<td>4.1</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>25.73</td>
<td>0.47</td>
<td>1.8</td>
<td>0.73</td>
<td>2.9</td>
</tr>
<tr>
<td>Panel 1</td>
<td>1</td>
<td>80</td>
<td>4.78</td>
<td>0.19</td>
<td>4.0</td>
<td>0.30</td>
<td>6.3</td>
</tr>
<tr>
<td>Panel 2</td>
<td>1</td>
<td>80</td>
<td>11.03</td>
<td>0.13</td>
<td>2.8</td>
<td>0.18</td>
<td>3.8</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>80</td>
<td>10.89</td>
<td>0.13</td>
<td>1.2</td>
<td>0.23</td>
<td>2.1</td>
</tr>
<tr>
<td>Panel 3</td>
<td>1</td>
<td>80</td>
<td>17.60</td>
<td>0.43</td>
<td>2.4</td>
<td>0.77</td>
<td>4.4</td>
</tr>
<tr>
<td>Panel 4</td>
<td>1</td>
<td>80</td>
<td>35.40</td>
<td>0.79</td>
<td>2.2</td>
<td>1.19</td>
<td>3.4</td>
</tr>
<tr>
<td>Panel 5</td>
<td>1</td>
<td>80</td>
<td>41.84</td>
<td>0.71</td>
<td>1.7</td>
<td>1.35</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Representative data; results in individual laboratories may vary from these data.
Dilution
The ARCHITECT Homocysteine assay is designed to have a mean recovery of 100 ± 15% of the expected result for diluted specimens. A dilution study was performed by diluting high concentration homocysteine EDTA plasma specimens with ARCHITECT Wash Buffer. The concentration of homocysteine was determined for each dilution of sample using the ARCHITECT Homocysteine assay, and the resulting percent recovery was calculated. A subset of the dilutions that were performed on each sample from this study are summarized in the following table. Mean recovery across the entire set of dilutions for each sample equals 103.9%, 106.2%, and 104.1%, respectively, for samples 1, 2, and 3 shown below.*

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Dilution Factor</th>
<th>Expected Value (μmol/L)</th>
<th>Mean Observed Value (μmol/L)</th>
<th>% Recoverya</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Undiluted</td>
<td>41.97</td>
<td>41.97</td>
<td>--</td>
</tr>
<tr>
<td>1:1.25</td>
<td>2.099</td>
<td>34.11</td>
<td>101.6</td>
<td></td>
</tr>
<tr>
<td>1:10</td>
<td>8.39</td>
<td>9.07</td>
<td>108.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.20</td>
<td>4.62</td>
<td>110.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Undiluted</td>
<td>44.23</td>
<td>44.23</td>
<td>--</td>
</tr>
<tr>
<td>1:1.25</td>
<td>35.38</td>
<td>38.31</td>
<td>102.6</td>
<td></td>
</tr>
<tr>
<td>1:2</td>
<td>22.11</td>
<td>22.81</td>
<td>103.1</td>
<td></td>
</tr>
<tr>
<td>1:5</td>
<td>8.85</td>
<td>9.98</td>
<td>112.8</td>
<td></td>
</tr>
<tr>
<td>1:10</td>
<td>4.42</td>
<td>5.15</td>
<td>116.5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Undiluted</td>
<td>45.79</td>
<td>45.79</td>
<td>--</td>
</tr>
<tr>
<td>1:1.25</td>
<td>36.63</td>
<td>36.55</td>
<td>99.8</td>
<td></td>
</tr>
<tr>
<td>1:2</td>
<td>22.90</td>
<td>23.56</td>
<td>102.9</td>
<td></td>
</tr>
<tr>
<td>1:5</td>
<td>9.16</td>
<td>10.35</td>
<td>113.1</td>
<td></td>
</tr>
<tr>
<td>1:10</td>
<td>4.58</td>
<td>4.94</td>
<td>107.8</td>
<td></td>
</tr>
</tbody>
</table>

a % Recovery = \( \frac{\text{Mean Observed Value (μmol/L)}}{\text{Mean Expected Value (μmol/L)}} \times 100 \)

* Representative data; results in individual laboratories may vary from these data.

Autodilution Verification
Recovery performance was evaluated for the 1:10 autodilution method of the ARCHITECT Homocysteine assay versus the 1:10 manual dilution method using three human EDTA plasma specimens with homocysteine levels that were greater than the ARCHITECT Homocysteine Calibrator F (50.0 μmol/L). Two replicates each of the autodiluted and manually diluted sample were assayed on one instrument using the ARCHITECT Homocysteine assay. The percent recovery results are summarized in the following table.*

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Automated Diluted Value (μmol/L)</th>
<th>Manually Diluted Value (μmol/L)</th>
<th>% Recoverya</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40.19</td>
<td>44.06</td>
<td>91.2</td>
</tr>
<tr>
<td>2</td>
<td>41.10</td>
<td>44.85</td>
<td>91.6</td>
</tr>
<tr>
<td>3</td>
<td>40.56</td>
<td>44.46</td>
<td>91.2</td>
</tr>
</tbody>
</table>

a % Recovery = \( \frac{\text{Mean Automated Diluted Value (μmol/L)}}{\text{Mean Manually Diluted Value (μmol/L)}} \times 100 \)

* Representative data; results in individual laboratories may vary from these data.

Sensitivity
Sensitivity is defined as the limit of detection (LOD). The ARCHITECT Homocysteine assay is designed to have a limit of detection of ≤ 1.0 μmol/L. The limit of blank (LOB) and LOD of the ARCHITECT Homocysteine assay were determined based on guidance from the CLSI Protocol EP17-A30 using proportions of false positives (α) less than 5% and false negatives (β) less than 5%. These determinations were performed using one blank (120 replicates) and five low level homocysteine samples (40 replicates each); LOB = 0.30 μmol/L and LOD = 0.64 μmol/L.*

* Representative data; results in individual laboratories may vary from these data.

Specificity
The specificity of the ARCHITECT Homocysteine assay was determined by studying the cross-reactivity of compounds whose chemical structure or concurrent usage may potentially interfere with the ARCHITECT Homocysteine assay. A study based on guidance from CLSI Protocol EP7-A231 was performed for the ARCHITECT Homocysteine assay. Specificity of the assay was determined by spiking solutions of each of the following compounds into human EDTA plasma specimens with homocysteine values ranging from 4.83 μmol/L to 43.70 μmol/L. Mean percent cross-reactivity at the levels indicated for each compound are summarized in the following table.*

<table>
<thead>
<tr>
<th>Test Compound</th>
<th>Concentration (mM)</th>
<th>Mean % Cross-Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-Adenosyl-L-Methionine</td>
<td>0.5</td>
<td>11.78b</td>
</tr>
<tr>
<td>L-Cysteine</td>
<td>100</td>
<td>0.01</td>
</tr>
<tr>
<td>L-Cystathionine</td>
<td>0.5</td>
<td>0.30</td>
</tr>
<tr>
<td>Adenosine</td>
<td>5.0</td>
<td>0.72</td>
</tr>
<tr>
<td>Glutathione</td>
<td>100</td>
<td>0.003</td>
</tr>
<tr>
<td>Glutathione Thiolactone</td>
<td>0.25</td>
<td>3.22</td>
</tr>
</tbody>
</table>

b Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert.

* Representative data; results in individual laboratories may vary from these data.

Interference
Potential interference in the ARCHITECT Homocysteine assay from the following compounds is designed to have a mean recovery of 100 ± 10% of the expected homocysteine concentration at the levels indicated. Studies based on guidance from the CLSI Protocol EP7-A231 were performed for the ARCHITECT Homocysteine assay. EDTA plasma specimens with homocysteine levels across the assay range of 1.00 to 50.00 μmol/L were supplemented with the following potentially interfering compounds. The mean recovery observed in EDTA plasma specimens during these studies ranged from 94.4% to 104.5%.*

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>20 mg/dL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>1000 mg/dL</td>
</tr>
<tr>
<td>Low Protein</td>
<td>3 g/dL</td>
</tr>
<tr>
<td>High Protein</td>
<td>12 g/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>6000 mg/dL</td>
</tr>
<tr>
<td>Heparin</td>
<td>1 U/mL</td>
</tr>
</tbody>
</table>

* Representative data; results in individual laboratories may vary from these data.

Method Comparison
The ARCHITECT Homocysteine assay is designed to have a slope of 1.0 ± 0.1 and a correlation coefficient (r) of ≥ 0.90 for plasma samples when compared to AxSYM Homocysteine. A correlation study based on guidance from CLSI Protocol EP9-A232 was performed on 456 EDTA plasma specimens to compare the ARCHITECT Homocysteine assay to the AxSYM Homocysteine assay. Data from this study were analyzed using the Passing-Bablok method and are summarized in the following table and graph.*

<table>
<thead>
<tr>
<th>ARCHITECT Homocysteine vs. AxSYM Homocysteine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Observations</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>456</td>
</tr>
</tbody>
</table>

Specimen Range (ARCHITECT): 3.18 μmol/L to 49.39 μmol/L
Specimen Range (AxSYM): 3.70 μmol/L to 49.94 μmol/L

a A linear regression method with no special assumptions regarding the distribution of the samples and measurement errors.
ARCHITECT Homocysteine vs. AxSYM Homocysteine

* Representative data; variables such as differences in sampling size and sample population may impact the correlation of the assay, therefore, results in individual laboratories may vary from these data.

A bias analysis of ARCHITECT Homocysteine vs. AxSYM Homocysteine was performed on the same 456 Method Comparison specimens in the range of 3.70 to 49.94 μmol/L. The following representative data are provided to aid in understanding the difference between the two assays. The average percent bias exhibited by ARCHITECT vs. AxSYM in this study was -5.94%. The 95% confidence interval of that average percent bias is -6.77% to -5.12%. Results of the study are summarized in the following graph.*

ARCHITECT Homocysteine % Bias to AxSYM Homocysteine

* Representative data; results in individual laboratories may vary from these data.

BIBLIOGRAPHY


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