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

NOTE: Changes Highlighted

INTENDED USE
The MULTICRIT GENT Vario assay (CRPVA) is intended for the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma with variable assay ranges (CRP16, CRP32, CRP48) using the ARCHITECT i Systems.

SUMMARY AND EXPLANATION OF TEST
C-reactive protein (CRP) is an acute phase protein whose concentration rises non-specifically in response to inflammation. CRP is seen to increase as a result of the inflammatory process, most notably in response to pneumococcal (bacterial) infection, inflammatory disease, and a variety of other disease states. Individual variation in the rate of production of CRP may be seen among individuals. The most common source of CRP is the liver. There may be other sources of CRP as well, including the lung, heart, and pancreas. CRP has been shown to be a marker for inflammation and infection, in addition to serving as a monitor of patient response to pharmacological therapy and surgery.

PRINCIPLES OF PROCEDURE
MULTICRIT Vario is a latex immunoassay developed to accurately and reproducibly measure blood CRP levels in serum and plasma. When an antigen-antibody reaction occurs between CRP in a sample and anti-CRP antibody, which has been adsorbed to latex particles, agglutination results. This agglutination is detected as an absorbance change (572 nm), with the rate of change being proportional to the quantity of CRP in the sample. Three different methods (High Sensitivity [CRP16], Standard [CRP32], and Wide Range [CRP48]) are available to cover a wide analytical measurement range.

Methodology: Turbidometric/Immunoassay

REAGENTS
Reagent Kit

Storage:

CRP16: 2 x 37 mL
CRP32: 3 x 86 mL
CRP48: 3 x 86 mL

High sensitivity:

Control: 600
Standard: 2000
Wide range: 4000

Calculations are based on the minimum reagent kit volume per kit.

CAUTION:

Reagent bubbles may interfere with proper detection of reagent level in the cartridges, causing insufficient reagent aspiration that could impact results.

REAGENT HANDLING AND STORAGE (Continued)
Reagent Storage
- Unopened reagents are stable until the expiration date when stored at 2 to 8°C.
- Reagent stability is 60 days if the reagent is uncapped and onboard.

Indications of Deterioration
- Instability or deterioration should be suspected if there are visible signs of leakage, extreme turbidity, microbial growth, if calibration does not meet the appropriate package insert and/or ARCHITECT System Operations Manual criteria, or if controls do not meet the appropriate criteria.

WARNINGS AND PRECAUTIONS
Precautions for Users
- For in vitro diagnostic use.
- Do not use components beyond the expiration date.
- Do not mix materials from different lot numbers.
- It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens. 2, 3 Biohazard Level 2 or other appropriate biohazard practices should be used for materials that contain or are suspected of containing infectious agents.
- This product contains sodium azide; for a specific listing, refer to the REAGENT’S section of this package insert. Contact with azide liberates very toxic gas. This material and its container must be disposed of in a safe way.

NOTE: Refer to Section 6 of the ARCHITECT System Operations Manual for proper handling and disposal of reagents containing sodium azide.

SPECIMEN COLLECTION AND HANDLING
Suitable Specimens
- Serum: Use serum collected by standard venipuncture techniques into plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. If sample is stored before centrifugation, mix and centrifuge the specimen to remove particulates prior to testing.
- Plasma: Use plasma collected by standard venipuncture techniques into plastic tubes. Acceptable anticoagulants are lithium heparin (with or without gel barrier), sodium heparin, and EDTA. Ensure centrifugation is adequate to remove platelets. When processing samples, separate plasma from blood cells or gel according to the specimen collection tube manufacturer’s instructions.

NOTE: Glass tubes were not tested.

For total sample volume requirements, refer to the ASSAY PARAMETERS section of this package insert and Section 5 of the ARCHITECT System Operations Manual.

Specimen Storage

Temperature

Maximum Storage

Bibilographical Reference

July 2010

6K2630401_FU_01_EN

Distributed by

Abbott Laboratories Inc.
Abbott Park, IL 60064 USA
6550 Westlake Drive

65205 Wiesbaden, Germany

Guder et al. suggest storage of frozen specimens at -20°C for no longer than the time interval cited above. However, limitations of laboratory equipment make it necessary in practice for clinical laboratories to establish a range around 2°C for specimen storage. This temperature range may be established from either the freezer manufacturer’s specifications or your laboratory standard operating procedure(s) for specimen storage.

NOTE: Stained specimens must be respected for particulars. If present, mix and centrifuge the specimen to remove particulates prior to testing.
PROCEDURE

Materials Provided
- 6K26-30 MULTIGENT CRP Vario Kit
- 6K26-41 MULTIGENT CRP Vario Kit

Materials Required but not Provided
- 6K26-10 MUltIGENT CRP Calibrator Set
- 6K26-32 MULTIGENT CRP Calibrator Panel
- 6K26-12 MULTIGENT CRP Calibrator VIR
- 6K26-20 MULTIGENT CRP Kit
- 6K26-20 Immuno Control 1 (Not available in the US)
- 6K26-21 Immuno Control 2 (Not available in the US)
- 6K26-14 MULTIGENT CRP Calibrator HS
- 6K26-12 MULTIGENT CRP Calibrator WR

Refer to Appendix C of the ARCHITECT System Operations Manual for information on results calculations. To convert results from mg/dL to mg/L, multiply mg/dL by 10. 

Materials Required but not Provided
- 6K26-30 MULTIGENT CRP Vario Kit
- 6K26-41 MULTIGENT CRP Vario Kit

Materials Required but not Provided
- 6K26-10 MUltIGENT CRP Calibrator Set
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- 6K26-20 Immuno Control 1 (Not available in the US)
- 6K26-21 Immuno Control 2 (Not available in the US)
- 6K26-14 MULTIGENT CRP Calibrator HS
- 6K26-12 MULTIGENT CRP Calibrator WR

LIMITATIONS OF THE PROCEDURE

To convert results from mg/dL to mg/L, multiply mg/dL by 10. 

Representative performance data are given in the EXPECTED VALUES and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert. Results obtained in individual laboratories may vary.

LIMITATIONS OF THE PROCEDURE

The following are limitations on the use of the High Sensitivity CRP package insert:

Manufacturers recommendations.

CRP is not a substitute for traditional cardiovascular risk factors. 

Acute coronary syndrome management should not depend on CRP measurements.

Secondary prevention measures should not depend on CRP.

Serial measurements of CRP should not be used to monitor treatment.

The average of two CRP results; repeated optimally two weeks apart, should be used in monitoring disease activity.

For diagnostic purposes, the patient’s medical history and all other clinical findings should be considered when evaluating CRP results.

For detailed information on ordering dilutions, refer to Section 5 of the ARCHITECT System Operations Manual.

CALIBRATION

NOTE: The MULTIGENT CRP Vario assay must be calibrated using the individual levels listed in the ASSAY PARAMETERS. Refer to the parameters for the High Sensitivity CRP16, Standard CRP32, and Wide Range CRP48 methods and the MULTIGENT CRP Calibrator package insert specific for the method used in your laboratory.

Calibration is stable for approximately 15 days (360 hours) and is required with each change in reagent lot number. Verify calibration curve with at least two levels of controls according to the established quality control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

For a detailed description of how to calibrate an assay, refer to Section 6 of the ARCHITECT System Operations Manual.

QUALITY CONTROL

As appropriate, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions.

Two levels of controls (normal and abnormal) are to be run every 24 hours.

If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.

If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.

Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

RESULTS

Refer to Appendix C of the ARCHITECT System Operations Manual for information on results calculations.

Schnabel et al. have published pediatric reference ranges. CRP is an acute phase protein whose concentration rises non-specifically in response to inflammation. CRP values should not be interpreted without a complete clinical evaluation. Follow-up testing of patients with elevated values is recommended in order to help rule out a recent response to undetected infection or tissue injury. It is recommended that each laboratory establish its own expected range. For diagnostic purposes, the patient’s medical history and all other clinical findings should be considered when evaluating CRP results.

EXPECTED VALUES

Reference Range

<table>
<thead>
<tr>
<th>Method</th>
<th>Dilution</th>
<th>Range (mg/dL)</th>
<th>Range (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum and plasma</td>
<td>1.0</td>
<td>≤ 0.5</td>
<td>≤ 5</td>
</tr>
<tr>
<td>High sensitivity</td>
<td>2.0</td>
<td>0.1 to 16.00</td>
<td>0.1 to 160</td>
</tr>
<tr>
<td>Standard</td>
<td>2.0</td>
<td>0.2 to 32.00</td>
<td>0.2 to 320</td>
</tr>
<tr>
<td>Wide range</td>
<td>2.0</td>
<td>0.2 to 48.00</td>
<td>0.2 to 480</td>
</tr>
</tbody>
</table>

The MULTIGENT CRP Vario assay must be calibrated using the individual levels listed in the ASSAY PARAMETERS. Refer to the parameters for the High Sensitivity CRP16, Standard CRP32, and Wide Range CRP48 methods and the MULTIGENT CRP Calibrator package insert specific for the method used in your laboratory.

Interfering Substances

Interference studies were conducted using an acceptance criteria of ± 5% deviation from the target value. No interference was observed at the concentrations below.

<table>
<thead>
<tr>
<th>Interfering Substance</th>
<th>Interferent Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin, conjugated and free</td>
<td>30 mg/dL (53 μmol/L)</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>500 mg/dL (15 g/L)</td>
</tr>
<tr>
<td>Intraflud</td>
<td>1,500 mg/dL (50 g/L)</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>550 IU/mL (150 kU/L)</td>
</tr>
</tbody>
</table>

For detailed information on ordering dilutions, refer to Section 5 of the ARCHITECT System Operations Manual.

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Method Comparison (Continued)

SPECIFIC PERFORMANCE CHARACTERISTICS (Continued)

Precision
The precision of the MULTIGENT CRP Vari method is ≤ 5% Total CV. Studies were performed using CLSI protocol NCCLS EP1-A2. Representative results in mg/L are summarized below.

CRP High Sensitivity Method

<table>
<thead>
<tr>
<th>Method</th>
<th>MEAN</th>
<th>%CV</th>
<th>SPIE/95%</th>
<th>RANGES</th>
<th>Run controls for onboard reagents by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP Wide Range Method</td>
<td>5.10</td>
<td>18.30</td>
<td>73.30</td>
<td>319.40</td>
<td>Lot</td>
</tr>
<tr>
<td>CRP High Sensitivity Method</td>
<td>0.10</td>
<td>0.10</td>
<td>0.10</td>
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Method Comparison

Serum results from the MULTIGENT CRP Vari method on the ARCHITECT System were compared with the results from a commercially available nephelometric methodology. Serum results from the MULTIGENT CRP Vari method on an ARCHITECT System were compared with the results on the AEROSET System for the MULTIGENT CRP High Sensitivity method only, serum results from an ARCHITECT System and the AEROSET System were also compared with the results from a commercially available turbidimetric methodology. Method comparison data are presented in mg/L.

Method Comparison (Continued)

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CRP Wide Range Method

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<th>MEAN</th>
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