**Intended Use**
The Lp(a) reagent set is an in vitro diagnostic test for the quantitative determination of lipoprotein(a) [Lp(a)] in human serum and plasma samples on the Mindray BS-480. The measurement of Lp(a) is useful in assessing lipid metabolism disorders and atherosclerotic cardiovascular disease in specific populations, when used in conjunction with clinical evaluation and other lipoprotein tests.

**Summary and Explanation**
Lp(a) was discovered by K. Berg in 1963. Lp(a) is similar to low-density lipoprotein (LDL) in lipid composition but differs in protein profile. The structural component of Lp(a) distinguishing it from LDL and implicating it in the coronary disease process is apolipoproteins [apo(a)], a highly glycosylated protein attached by disulfide bond to apolipoprotein B100 [apo B100]. apo(a) has a high degree of structural homology with plasminogen that is a key zymogen of the coagulation cascade.

The similarity of structural components of Lp(a) to LDL and to plasminogen suggests that Lp(a) may be associated with atherosclerosis and/or thrombosis. Although there is a lack of consistency in the conclusions of the studies about the contributory role of Lp(a) to coronary heart disease, it is widely accepted that Lp(a) is an important risk factor that may contribute to coronary artery disease independently or cooperatively with other risk factors. While the wide differences in Lp(a) levels seen among individuals are largely due to hereditary factors, the identification of individuals at risk through diagnostic screening should nevertheless be useful in alerting them to the need to eliminate or control other high risk factors when possible.

Lp(a) values should be interpreted in conjunction with clinical evaluation and other lipoprotein tests when assessing atherosclerotic cardiovascular disease in specific populations.

**Principle of the Method**
This reagent set is a latex-enhanced immunoturbidimetric in vitro diagnostic assay. Lp(a) in the sample binds to the specific anti-Lp(a) antibody, which has been adsorbed to latex particles, and agglutinates. The agglutination is detected as an absorbance change when read on an automated chemistry analyzer. The magnitude of the change in absorbance is proportional to the quantity of Lp(a) in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from calibrators of known concentrations.

**Equipment and Materials Required but Not Provided**
Mindray BS-480 Analyzer, Physiological Saline, Quality Control Materials (MedTest DX Lipid Controls (Catalog Number: 3000))

**Storage and Handling**
Store reagents at 2 to 8 °C, while protecting from light. Once placed on board reagent is stable for 30 days. The reagents can be used any time before the expiration date indicated on the box label.

**Warnings, Precautions, and Hazards**
1. ** FOR IN VITRO DIAGNOSTIC USE ONLY**
2. Calibrators prepared from human sera have been tested as negative for HBs antigen, HIV 1/2 and HCV antibodies. As no test method can assure the complete absence of HIV, hepatitis B virus, hepatitis C virus or other infectious agents, patient samples and human based reagents should be handled with care and treated as potentially infectious and biohazardous.
3. Calibrators and reagents contain less than 0.1 w/v% sodium azide as a preservative. As sodium azide may react with lead and copper piping to form explosive metal azides, the calibrators and the reagents should be disposed by flushing with copious amounts of water.
4. All solutions supplied with the test kit should be handled carefully and disposed of properly.

**Hazards:**
- R1 and R2: Hazard Classifications: Not a hazardous substance or mixture.
- Pictogram and Signal Word: Not required.
- Precautionary Statements: Not a hazardous substance or mixture.

**Cautions**
1. It is recommended that each laboratory determine calibration frequency. Calibration is recommended after reagent lot change and as required following quality control procedures.
2. Samples containing high levels of Lp(a) (above the assay range) should be diluted with physiological saline and retested.
3. Do not use reagents after expiration date on the label.

**Sampling and Sampling Method**
1. After sampling, the test should be performed without delay. If the test cannot be done immediately, the sample should be placed in a tightly sealable container and stored at -20° C or below.
2. For serum samples, after the blood has clotted thoroughly, the sample is centrifuged and the serum is separated from blood cells and fibrins.
3. Plasmas collected with Disodium EDTA, Dipotassium EDTA, Sodium Heparin, Lithium Heparin or Citric acid can be used for the assay in addition to serum samples.

**Reagent Preparation**
1. No pretreatment is required for reagents or sample.
2. Calibrators are provided in 5 x 1 ml set. (Catalog Number: LPAC480)
3. Physiological saline may be required to dilute high Lp(a) samples. For physiological saline, dissolve 0.9g sodium chloride in distilled water and bring to a final volume of 100 mL.
Lipoprotein (a) Reagent Set

Establishing a calibration curve

Prepare a multi-point calibration curve using the Lp(a) Calibrator Set according to the specific application parameters. Under typical operating conditions manufacturer calibration stability studies have shown the calibration curve will be stable for at least 14 days. The Lp(a) concentration of the calibrators is given on each calibrator label. Note: Values for the calibrators in nmol/L are also available by contacting the MedTest DX Technical Service department.

Quality Control

It is recommended that commercially available controls with known concentrations be included in all assays.

Performance

The following performance data were obtained from testing on Mindray BS-480 analyzer using appropriate application parameters and calibration instructions.

1. Assay Range: 2.0-80.0 mg/dL.
2. 2.0 mg/dL was obtained by extrapolating +2.6SD value of the zero standard (saline) to the plot of the observed mean concentrations and ±2.6SD of serially diluted low Lp(a) pool. The linearity was assessed using equally spaced serial dilutions of Lp(a) control. Comparison of the observed concentrations to the concentrations calculated from the linear regression equation showed bias within plus or minus 5% up to a dilution over 80 mg/dL.
3. Correlation: A study was performed between the Mindray BS-480 and a similar analyzer using this method, resulting in the following:

<table>
<thead>
<tr>
<th>Method</th>
<th>Lp(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>83</td>
</tr>
<tr>
<td>Mean Lp(a) (mg/dL)</td>
<td>24.22</td>
</tr>
<tr>
<td>Range (mg/dL)</td>
<td>3.7-77.7</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>20.20</td>
</tr>
<tr>
<td>Regression Analysis</td>
<td>y = 0.996x + 1.60</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.969</td>
</tr>
</tbody>
</table>

4. Precision: Precision studies were performed following a modification of the guidelines contained in the NCCLS document EP5-T2.

<table>
<thead>
<tr>
<th>Sample</th>
<th>LOW</th>
<th>MID</th>
<th>HIGH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>Mean</td>
<td>14.58</td>
<td>33.82</td>
<td>61.28</td>
<td>60</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>0.62</td>
<td>0.54</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>Coefficient of Variation (%)</td>
<td>4.4%</td>
<td>1.6%</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

5. Sensitivity: 2SD limit of detection (95% Conf) = 0.2 mg/dL.
6. Specificity: When sera containing known levels of Lp(a) in the assay range were measured, the values obtained for the sera were in the range of the known concentrations, plus or minus 10%.
7. Sample Types: Plasma samples drawn with each of EDTA, Heparin and Citrate and serum samples from 50 subjects were evaluated on Hitachi 917 Automated analyzer using this Lp(a) reagent and calibrators. Results of the comparison study showed that serum and plasma samples can provide substantially the same Lp(a) values.

<table>
<thead>
<tr>
<th>Serum</th>
<th>EDTA (2Na)</th>
<th>EDTA (2K)</th>
<th>Heparin (Na)</th>
<th>Heparin (Li)</th>
<th>Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>13.5</td>
<td>13.0</td>
<td>13.2</td>
<td>11.1</td>
<td>11.0</td>
</tr>
<tr>
<td>Mean</td>
<td>16.44</td>
<td>16.00</td>
<td>16.21</td>
<td>15.22</td>
<td>14.51</td>
</tr>
<tr>
<td>Minimum</td>
<td>2.0</td>
<td>1.7</td>
<td>1.8</td>
<td>2.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>81.1</td>
<td>78.8</td>
<td>79.5</td>
<td>78.3</td>
<td>77.3</td>
</tr>
<tr>
<td>SD</td>
<td>15.1</td>
<td>14.7</td>
<td>14.8</td>
<td>14.5</td>
<td>14.5</td>
</tr>
</tbody>
</table>

8. Expected Values: 30 mg/dL was used as a cut-off point or threshold value in some previous studies. A study of 190 samples obtained from an ambulatory population with no history of CAD (120 males and 70 females) was performed and found a comparable normal range (4.0 to 27.4 mg/dL). Mean age of the males was 33.6 (ranged from 20 to 51) and mean age of the females was 28.8 (ranged from 21 to 43). There was no substantial
difference in Lp(a) levels between the males and the females. Means and SDs were 15.5 mg/dL and 21.6 mg/dL in the males and 18.3 mg/dL and 17.6 mg/dL in the females, respectively.

Reference ranges have not been established for this assay for different ethnic populations or disease states. Since Lp(a) levels are largely influenced by hereditary factors and vary with ethnic population, it is recommended that each laboratory establish its own expected values.

Lp(a) values should be interpreted in conjunction with clinical evaluation and other lipoprotein tests when assessing atherosclerotic cardiovascular disease in specific populations.

References
**CHEMISTRY PARAMETERS**

<table>
<thead>
<tr>
<th>Chem:</th>
<th>Lp(a)</th>
<th>No.:</th>
<th>225</th>
<th>Sample Type:</th>
<th>Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemistry:</td>
<td>Lipoprotein(a)</td>
<td>Print Name:</td>
<td>Lp(a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction Type:</td>
<td>Fixed Time</td>
<td>Reaction Direction:</td>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pri Wave:</td>
<td>660</td>
<td>Sec Wave:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit:</td>
<td>mg/dL</td>
<td>Decimal</td>
<td>0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blank Time:</td>
<td>47 49</td>
<td>Reaction Time:</td>
<td>54 71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sample Vol.**  | **Aspirated** | **Diluent** | **Reagent Vol.** | **Diluent**
--- | --- | --- | --- | ---
Standard: | 3.7 ul | --- ul | --- ul | R1: 120 ul | --- ul |
Decreased: | --- ul | --- ul | --- ul | R2: 40 ul | --- ul |
Increased: | --- ul | --- ul | --- ul | R3: --- ul | --- ul |

☐ Sample Blank  ☐ Auto Rerun  

**Slope/Offset Adjustment**

Slope: 1  Offset: 0

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**Linearity Range (Standard)**  | 2.0  | 80.0  |
--- | --- | --- |
**Linearity Range (Decreased)**
--- | --- | --- |
**Linearity Range (Increased)**
--- | --- | --- |
**R1 Blank Abs:**
--- | --- | --- |
**Blank Response:**
--- | --- | --- |
**Uncapping Time**
--- | --- | --- |
**Reagent Alarm Limit:**
☐ Enzyme Linear Extension

☐ Prozone Check  ○ Rate Check  ○ Antigen Addition

Q1:  Q2:  Q3:  Q4:
PC:  ABS:
### CALIBRATION PARAMETERS

**Calibrator Definition**

<table>
<thead>
<tr>
<th>Calibrator</th>
<th>Lot No.</th>
<th>Exp Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

**Carousel**

| Sample Carousel 1 | * |
| Sample Carousel 2 | * |
| Sample Carousel 3 | * |

**Reagent/Calibration**

<table>
<thead>
<tr>
<th>Calibrator</th>
<th>Pos</th>
<th>Lot No.</th>
<th>Exp Date</th>
<th>Chem</th>
<th>Conc</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>W</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Lp(a) Cal 1</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Lp(a) Cal 2</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Lp(a) Cal 3</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Lp(a) Cal 4</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Lp(a) Cal 5</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Lp(a)</td>
<td>*</td>
<td>mg/dL</td>
</tr>
</tbody>
</table>

**Calibration Setup**

| Chem: Lp(a) |

**Calibration Settings**

| Math Model: Spline | Replicates: 2 |

**Acceptance Limits**

| Cal Time: * Hour | Slope Diff: --- SD: --- |
| Sensitivity: --- Repeatability: --- |
| Deter Coeff: --- |

**Auto Calib:**

- Bottle Changed
- Lot Changed
- Cal Time

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It is recommended that two levels of control material be assayed daily.

* Indicates user defined parameter.

**Symbol Key**

- Use by (YYYY-MM-DD)
- Lot and batch code
- Catalog number
- Manufacturer
- Temperature limitation
- Consult instructions for use
- In vitro diagnostic medical device

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