BIOPHEN™ Plasma Calibrator

INTENDED USE:
BIOPHEN™ Plasma Calibrator is normal citrated human plasma used as the calibrator in the assay methods for coagulation factors Antithrombin and Protein C.

The following table shows the various parameters, which are measured using assays from HYPHEN BioMed or from other manufacturers, and according to the package inserts:

<table>
<thead>
<tr>
<th>Assays</th>
<th>Reagents</th>
<th>Manufacturers</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin</td>
<td>BIOPHEN™</td>
<td>Hyphen BioMed</td>
<td>221100</td>
</tr>
<tr>
<td></td>
<td>Antithrombin</td>
<td></td>
<td>221105</td>
</tr>
<tr>
<td>Protein C</td>
<td>BIOPHEN™</td>
<td>Hyphen BioMed</td>
<td>221200</td>
</tr>
<tr>
<td></td>
<td>Protein C</td>
<td></td>
<td>221205</td>
</tr>
<tr>
<td>Lupus Anticoagulant</td>
<td>DVVtest/DVVconfirm®</td>
<td>Biomedica Diagnostics</td>
<td>810 / 815L</td>
</tr>
</tbody>
</table>

DVVtest, DVVconfirm are registered trade marks from Biomedica Diagnostics Inc.

The BIOPHEN™ Plasma Calibrator is tested for the absence of Lupus Anticoagulant and can be used for this investigation.

REAGENT:
CAL: Calibrator : Normal citrated human plasma, lyophilized.
12 vials of 1 mL.

The calibrator concentrations may vary slightly from one batch to the next. For the assay, see the exact values provided on the flyer provided with the kit used.

The following table shows the usual expected level for the BIOPHEN™ Plasma Calibrator.

<table>
<thead>
<tr>
<th>Assays</th>
<th>Reagents</th>
<th>Expected level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin</td>
<td>BIOPHEN™</td>
<td>&gt; 85%</td>
</tr>
<tr>
<td></td>
<td>Antithrombin</td>
<td></td>
</tr>
<tr>
<td>Protein C</td>
<td>BIOPHEN™</td>
<td>&gt; 85%</td>
</tr>
<tr>
<td></td>
<td>Protein C</td>
<td></td>
</tr>
<tr>
<td>Lupus Anticoagulant</td>
<td>DVVtest/DVVconfirm®</td>
<td>≤ 1.20</td>
</tr>
</tbody>
</table>

WARNS AND PRECAUTIONS:
- Calibrator plasma contains stabilizing agents.
- Each pouch of human plasma used for kit preparation was obtained from healthy donors. Each plasma used was screened for the presence of the HBs antigen, of anti-HIV1, anti-HIV2 and anti-HCV antibodies, using approved methods, and found to be negative. Nevertheless, no tests can totally exclude the presence of infectious agents. For this reason, any precaution required for the use of potentially infectious products should be taken when handling and disposing of plasma.
- Waste should be disposed of in accordance with applicable local regulations.
- Handle the reagents with care 
- Avoid contamination during use. If possible, avoid reagent evaporation during use by limiting the liquid-air exchange surface. Evaporation reduces the reagent's stability in the analyzer.
- To ensure reagent stability, seal the vials after use with their respective caps, or close the plastic micro-containers into which the plasmas may have been transferred, depending on the protocol used.
- Aging studies, conducted over a 3-week period at 30 °C, show that the reagents can be shipped at room temperature over a short period of time, without degradation.
- It is recommended to homogenize each vial before use, in order to have a good reproducibility, all the time.
- For in vitro diagnostic use.

REAGENT PREPARATION AND STABILITY:
The reagents are lyophilized under a vacuum in their vials. To avoid any product loss when opening the vial, gently remove the freeze-drying stopper.

CAL: Calibrator : Normal citrated human plasma
Reconstitute the contents of each vial with exactly 1 mL distilled water, shake vigorously until fully dissolved. Allow to stabilize for 30 min. at room temperature (18-25 °C), shaking occasionally. Homogenize prior to use.

Reagent stability after reconstitution, free from any contamination or evaporation, and stored in the original vial, is of:
- 24 hours at 2-8°C.
- 8 hours at room temperature (18-25 °C).
- Do not freeze.

STORAGE CONDITIONS:
Unopened reagents should be stored at 2-8°C in their original packaging. Under these conditions, they can be used until the expiry date printed on the kit.

English, Last revision: 03-2018

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED:
Reagents:
- Distilled water.

Materials:
- Calibrated pipettes.

TRACEABILITY:
The value assignment of the various parameters reported is related to the corresponding International Standards, when available, or against an internal reference.

PROPERTIES:
BIOPHEN™ Plasma Calibrator can be used for the calibration of some coagulation assays (especially Antithrombin and Protein C). The use of quality controls serves to validate method compliance, along with between-series assay homogeneity for a given batch of reagents. Include the quality controls with each series, as per good laboratory practice, in order to validate the test.

A new calibration curve should be defined, preferably for each test series, and at least for each new reagent batch, or after analyzer maintenance, or when the measured quality control values fall outside the acceptable range for the method.

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PERFORMANCE:
The following values, obtained for one lot of BIOPHEN™ Plasma Calibrator, are provided as an example only.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Concentration</th>
<th>N</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin</td>
<td>100%</td>
<td>18</td>
<td>1.50</td>
</tr>
<tr>
<td>Protein C</td>
<td>96%</td>
<td>18</td>
<td>1.45</td>
</tr>
<tr>
<td>DVVtest/DVVconfirm ratio</td>
<td>1.01</td>
<td>2</td>
<td>/</td>
</tr>
</tbody>
</table>

For each parameter, the concentration may present variations from lot to lot, but it is exactly measured for each lot and reported on the flyer provided within the kit.

W hen the BIOPHEN™ Plasma Calibrator is used for calibrating the assay of some coagulation factors, the BIOPHEN™ Plasma Calibrator is used for calibrating the assay of some coagulation factors, the BIOPHEN™ quality control plasma (BIOPHEN™ Normal Control Plasma, ref 223201, and BIOPHEN™ Abnormal Control Plasma, ref 223301) can be used in order to obtain an homogeneous quality control system. The values obtained for quality control plasmas must be within the acceptance ranges reported for the lot used or within range defined by the end user, in order to validate the test series. Should the value be out of these ranges, the results for the corresponding series must be considered as invalid. It is then recommended to rerun the series and to check all the assay parameters.

LIMITATIONS:
- Like all lyophilized plasmas, calibration plasmas are more or less turbid once resuspended. This turbidity is mainly due to plasma lipids that, after freeze-drying, become "less" soluble and may form a slight deposit.
- Any plasma displaying a coagulum or showing signs of bacterial or fungal contamination must be rejected.
- The calibrators are used under measurement conditions other than those validated by HYPHEN Biomed, the test results may vary. The laboratory is responsible for validating the use of these calibrators in its own analytical system.
- If necessary, let each vial stand 10 minutes at room temperature and shake gently before use in order to homogenize the contents.

SYMBOLS:
Symbols used and signs listed in the ISO 15223-1 standard, see Symbol definitions document.