Infinity™ ACE Liquid Stable Reagent
(Angiotensin Converting Enzyme)

PRODUCT SUMMARY

<table>
<thead>
<tr>
<th>Stability</th>
<th>Until Expiry at 2-8°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear Range</td>
<td>1 - 120 U/L</td>
</tr>
<tr>
<td>Specimen Type</td>
<td>Serum or Plasma</td>
</tr>
<tr>
<td>Method</td>
<td>Kinetic/Rate</td>
</tr>
<tr>
<td>Reagent Preparation</td>
<td>Supplied ready to use.</td>
</tr>
</tbody>
</table>

INTENDED USE

This reagent is intended for the in vitro quantitative determination of Angiotensin Converting Enzyme (ACE, EC3.4.15.1, dipeptidyl carboxypeptidase I) in human serum or plasma.

CLINICAL SIGNIFICANCE

ACE is a halide activated membrane bound exopeptidase that has a central role in the control of blood pressure. ACE catalyses the conversion of Angiotensin I to the powerful vasoconstrictor Angiotensin II and also inactivates circulating Bradykinin. ACE is present in the vascular beds of most organs, however, the highest levels are found in the endothelial cells of pulmonary capillaries. Lung ACE is considered to be the principal source of the serum enzyme.

The presence (I) or absence (D) of a 287 base pair fragment on the gene for ACE gives rise to three ACE genotypes, II, DD and ID. Since the discovery of the I/D polymorphism, further studies have shown that serum ACE activity is influenced by genotype. DD individuals have nearly twice the ACE activity of II individuals, with values from ID individuals being intermediate.

The measurement of serum ACE is widely used to aid in the differential diagnosis of clinically active pulmonary Sarcoidosis and for monitoring the effectiveness of steroid therapy. ACE measurement is also becoming widely used for monitoring the effects of ACE inhibitors in the treatment of hypertension and heart failure.

METHODOLOGY

Early methods for measuring ACE activity used the natural substrate Angiotensin I and products of the reaction were detected by bioassay, spectrophotoemtric and spectrofluorimetric assays for ACE, however, these methods were still not ideally suited to automated analysis.

The Infinity ACE reagent is based on the method first described by Holmquist et al. In this method the direct substrate N-[3-(2-furyl)-acryloyl] – L-phenylhistidyl-L-leucine as a substrate led to the development of more manageable spectrophotometric and sepectrofluorimetric assays for ACE, however, these methods were still not ideally suited to automated analysis.

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NOTE

1. The reagent and sample volumes may be altered proportionally to accommodate different spectrophotometer requirements.
CALIBRATION
Calibration is required. Thermo ACE calibrator (TR85201) is recommended. For calibration frequency on automated instruments refer to the instrument manufacturer's specifications. However, calibration stability is contingent upon optimum instrument performance and the use of reagents which have been stored as recommended in the stability and storage section of this package insert.
Recalibration is recommended at anytime if one of the following events occurs:
- The lot number of reagent changes.
- Preventative maintenance is performed or a critical component is replaced.
- Control values have shifted or are out of range and a new vial of control does not rectify the problem.

QUALITY CONTROL
To ensure adequate quality control, normal and elevated control should be run as unknown samples:-
- At least every eight hours.
- When a new bottle of reagent is used.
- After preventative maintenance is performed or a critical component is replaced.
Control results falling outside the upper or lower limits of the established ranges indicate the assay may be out of control. The following corrective actions are recommended in such situations:-
- Repeat the same controls.
- If repeated control results are outside the limits, prepare fresh control serum and repeat the test.
- If results are still out of control, recalibrate with fresh calibrator, then repeat the test.
- If results are still out of control, perform a calibration with fresh reagent, then repeat the test.
- If results are still out of control, contact Technical Services or your local distributor.

LIMITATIONS
1. Studies to determine the level of interference from haemoglobin, bilirubin and lipaemia were carried out. The following results were obtained:
   - **Haemoglobin:** No interference from haemoglobin up to 725 mg/dL.
   - **Free Bilirubin:** No interference from free bilirubin up to 222 µmol/L (13 mg/dL).
   - **Conjugated Bilirubin:** No interference from conjugated bilirubin up to 342 µmol/L (20 mg/dL).
   - **Lipaemia:** No interference from lipaemia, measured as triglycerides, up to 11.3 mmol/L (1000 mg/dL).
2. For a more comprehensive review of factors affecting ACE assays refer to the publication by Young.³
3. ACE inhibitors, such as Captopril and Teprotides will inhibit serum ACE activity.²,⁵
4. ACE is inhibited by EDTA.⁵

EXPECTED VALUES
At 37°C 8 - 52 U/L

The quoted values should serve as a guide only. It is recommended that each laboratory verify this range or derive a reference interval for the population it serves.⁷

PERFORMANCE DATA
The following data was obtained using the Infinity ACE Liquid Stable Reagent on a well maintained automated clinical chemistry analyser. Users should establish product performance on their specific analyser used.

IMPRECISION
Imprecision was evaluated over a period of 20 days using two levels of commercial control and following the NCCLS EPS-T procedure.⁶

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<thead>
<tr>
<th></th>
<th>LEVEL I</th>
<th>LEVEL II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of data points</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Mean (U/L)</td>
<td>35</td>
<td>90</td>
</tr>
<tr>
<td>SD (U/L)</td>
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<tr>
<td>CV (%)</td>
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<td>2.3</td>
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</table>

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</tr>
<tr>
<td>Mean (U/L)</td>
<td>35</td>
<td>90</td>
</tr>
<tr>
<td>SD (U/L)</td>
<td>3.7</td>
<td>5.1</td>
</tr>
<tr>
<td>CV (%)</td>
<td>10.8</td>
<td>5.7</td>
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ACCURACY
Comparison studies were carried out using a similar commercially available reagent as a reference. Serum samples were assayed in parallel and the results compared by least squares regression. The following statistics were obtained.

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<tr>
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</thead>
<tbody>
<tr>
<td>Number of sample pairs</td>
<td>108</td>
<td></td>
</tr>
<tr>
<td>Range of sample results</td>
<td>1 - 114 U/L</td>
<td>39.2 U/L</td>
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<tr>
<td>Mean of reference method results</td>
<td>34.3 U/L</td>
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<tr>
<td>Slope</td>
<td>0.961</td>
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<tr>
<td>Intercept</td>
<td>-3.3 U/L</td>
<td></td>
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<tr>
<td>Correlation coefficient</td>
<td>0.966</td>
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</tbody>
</table>

LINEARITY
When run as recommended the assay is linear between 1 and 120 U/L of ACE.

SENSITIVITY
When run as recommended the sensitivity of this assay is 0.084 µmA/min per U/L (1cm light path, 340nm).

REFERENCES

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Reorder Information and Technical Support
Catalogue No. | Configuration
--- | ---
TR85056 | 2 x 28 mL
TR85021 | 2 x 125 mL
TR85101 | Control 6 x 1 mL
TR85201 | Calibrator 6 x 1 mL

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