### ABSTRACT

New technologies are being developed that can precisely measure low concentrations of cardiac troponin I (cTnI) and T (cTnT) to assist in the clinical setting of ischemia, myocardial infarction (MI). Clinical implementation of hs-cTn assays, providing earlier diagnosis and improved therapies predicated on improved patient outcomes.

Cardiac troponin I (cTnI) and T (cTnT) are the preferred biomarkers for detection of myocardial injury and in the clinical setting of ischemia, myocardial infarction (MI). New technologies are being developed that can precisely measure low concentrations of cTnI in serum and plasma of normal, reference subjects. Such studies with high sensitivity troponin-I assays are essential for early detection of cardiac disease and management of patients presenting with symptoms suggestive of acute coronary syndrome.

The purpose of this study was to determine the serum 99th percentile reference value for the high sensitive singleplex cardiac troponin I assay.

### INTRODUCTION

Cardiac troponin I (cTnI) and T (cTnT) are the preferred biomarkers for detection of myocardial injury and in the clinical setting of ischemia, myocardial infarction (MI). New technologies are being developed that can precisely measure low concentrations of cTnI in serum and plasma of normal, reference subjects. Such studies with high sensitivity troponin-I assays are essential for early detection of cardiac disease and management of patients presenting with symptoms suggestive of acute coronary syndrome.

### METHODS

- **IBR approved obtained**
- **Healthy adult volunteers recruited to donate blood and complete a health questionnaire.**
- **Inclusion criteria:**
  - ≥18 yrs of age or older
  - No current or previous history of coronary artery disease or heart conditions
  - No current or previous history of cardiac related medical conditions including diabetes mellitus, hypertension, heart failure, hyperlipidemia or renal disease.
  - Not taking any medications for cardiac related medical conditions.
- **Serum samples** were processed, aliquoted and stored frozen at -70°C until day of analysis.
- **Aliquots of serum samples** were provided frozen to Singulex, where the Erenna assay system (microtiter plate system) measurement of cTnI was performed by the manufacturer, in triplicate.
- **All aliquots with were assayed by Dr. Apple’s research lab using the Roche Elecsys 2010 NT-proBNP assay to assist in defining normality of the subjects recruited.**
- **Non-parametric analysis for determination of the 99th percentiles, based on age and gender, was determined along CLSI guideline C28-A3.**
- **Statistical significance was accepted at the 0.05 level & all tests were two-tailed.**

### RESULTS

#### 99th Percentile Reference Value for the High Sensitive Singleplex Cardiac Troponin I Assay

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
<th>99th Percentile</th>
<th>Mean (95% CI)</th>
<th>Range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>348</td>
<td>10.19 (1.15, 1.73)</td>
<td>0.20 to 34.95</td>
<td></td>
<td>0.108</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>186</td>
<td>16.58 (1.72, 2.27)</td>
<td>0.20 to 34.95</td>
<td></td>
<td>0.108</td>
</tr>
<tr>
<td>Female</td>
<td>162</td>
<td>9.36 (1.04, 1.65)</td>
<td>0.20 to 34.95</td>
<td></td>
<td>0.108</td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 - 30 yrs</td>
<td>105</td>
<td>9.49 (1.37, 0.86)</td>
<td>0.20 to 29.05</td>
<td></td>
<td>0.108</td>
</tr>
<tr>
<td>31 - 50 yrs</td>
<td>134</td>
<td>16.58 (1.00, 2.06)</td>
<td>0.20 to 34.95</td>
<td></td>
<td>0.108</td>
</tr>
<tr>
<td>&gt;57 yrs</td>
<td>99</td>
<td>9.36 (1.45, 1.06)</td>
<td>0.20 to 34.95</td>
<td></td>
<td>0.108</td>
</tr>
</tbody>
</table>

### CONCLUSIONS

- cTnI measured by the high sensitivity Erenna cTnI assay measures 100% of normal subjects, allowing prospective diagnostic and risk assessment studies to be performed.
- Such studies with high sensitivity troponin-I assays are essential for early detection of cardiac disease and management of patients presenting with symptoms suggestive of acute coronary syndrome.
- As a research assay, the high sensitivity Singulex Erenna cTnI assay should be very useful in both clinical and preclinical studies.