TEST CODE:  
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J254-4</td>
<td>PSA Reflex to 4Kscore ≥ 1.5 ng/mL;</td>
</tr>
<tr>
<td></td>
<td>J264-3 - PSA Reflex to 4Kscore ≥ 3 ng/mL;</td>
</tr>
<tr>
<td>K136-2</td>
<td>PSA, Total &amp; Free Reflex to 4Kscore ≥ 1.5 ng/mL;</td>
</tr>
<tr>
<td>K135-4</td>
<td>PSA, Total &amp; Free Reflex to 4Kscore ≥ 3 ng/mL;</td>
</tr>
<tr>
<td>J148-8</td>
<td>4Kscore Test</td>
</tr>
</tbody>
</table>

**Methodology**  
Immunoassay

**Specimen Requirements**  
4 mL serum (SST)

**Collection Instructions**  
Fill tube, invert gently 2-3 times, let stand for 20 minutes, spin for 10-15 minutes and label with patient name

**Storage Instructions**  
Refrigerated

**Specimen Stability**  
3 Days

**Turnaround Time**  
3 days

**TEST BACKGROUND**
The 4Kscore Test incorporates measured blood levels of 4 kallikrein proteins: Total PSA (tPSA), Free PSA (fPSA), Intact PSA (iPSA), and human Kallikrein-2 (hK2) plus clinical information [age, digital rectal examination (DRE), and prior biopsy history] into a proprietary algorithm to calculate an individual man’s percent risk of aggressive prostate cancer if a prostate biopsy were performed. Intact PSA and hK2 biomarkers have consistently been found to be elevated in men with aggressive prostate cancer versus men with indolent prostate cancer or benign prostate conditions.

**CLINICAL UTILITY**
- Evaluates the risk of aggressive prostate cancer following a suspicious or abnormal PSA or DRE result
- Reduces prostate biopsies by identifying patients who can be safely monitored - patients with a low 4Kscore (≤ 7.5%) have a 98-99% chance to be without prostate cancer metastases within 20 years of long term follow-up
- Helps avoid costly and unnecessary treatment of indolent prostate cancer, saving the United States health care system an estimated $3 billion annually

**CLINICAL VALIDITY**
The 4Kscore Test accurately determines which patients with abnormal PSA and/or DRE would have aggressive (Gleason 7 or greater) prostate cancer if a prostate biopsy were performed. Test accuracy is illustrated in Figure 1. The average Area Under Curve (AUC) for predicting high-grade pathology on biopsy is 0.85 (range 0.80-0.90) for the 4Kscore Test and 0.66 (range 0.51-0.77) for Total PSA and DRE.
CLINICAL PERFORMANCE
Use of the 4Kscore Test allows providers to accurately identify a patient’s percent risk of aggressive prostate cancer if a prostate biopsy were performed and improve healthcare outcomes by only performing prostate biopsies on men who are at risk for aggressive prostate cancer. Performance of the 4Kscore test was validated in over 22,000 patients and reported in 12 peer-reviewed publications. These large retrospective and prospective studies show that use of the 4Kscore test could have, on average, avoided 45% of prostate biopsies.4-11

The 4Kscore Test not only predicts the risk for high-grade prostate cancer on biopsy, but it has also been shown to predict risk for distant prostate cancer metastases occurring up to 20 years later from a blood sample in otherwise healthy men who have PSA ≥ 2ng/mL. A population-based cohort in Västerbotten, Sweden followed 12,542 men to determine their risk of distant prostate cancer metastases. Results, as illustrated in Figure 2, show that a group of men who had a 4Kscore of 7.5% or lower were found to have 1% chance of developing metastatic prostate cancer by year 15.1

APPROPRIATE PATIENT PROFILE

Men who have:
- A suspicious or abnormal PSA
- Never had a diagnosis of prostate cancer
- Not taken 5-alpha reductase inhibitors within the last 6 months
- Not undergone any invasive urological procedure that may be associated with secondary PSA elevation within the last 6 months
- Not received a DRE in the previous 96 hours (4 days) before phlebotomy (DRE after phlebotomy is acceptable)

METHOD
Total PSA and Free PSA are measured using FDA-approved kits from Roche Diagnostics which uses quantitative electrochemiluminescence (ECLIA) methodology. The BioReference proprietary assays, Intact PSA and hK2, are laboratory developed tests validated by BioReference and are run on the auto-DELFIA by Perkin-Elmer and uses DELFIA (dissociation-enhanced lanthanide fluorescent immunoassay) methodology.

RESULTS INTERPRETATION
Based on the 4Kscore Test US validation study, prostate biopsy should be considered in most men with a 4Kscore result of 7.5% or higher. Reference ranges are as follows:
- Low Risk: 4Kscore result <7.5%
- Intermediate Risk: 4Kscore result 7.5-19%
- High Risk: 4Kscore result ≥20%

Patient management should be based on clinical judgment. Other clinical information (health status, medical history, family history of prostate cancer, PSA history, etc.) along with the 4Kscore Test result should be considered in the shared physician and patient decision regarding biopsy.

REFERENCES (For references 4-11, please ask your sales representative for adjunct Clinical Experience sheet)
3. Parekh DJ, Pursen Sm, Sjoberg DDm et al. A Multi-institutional Prospective Trial in the USA Confirms that the 4Kscore Accurately Identifies Men with High-grade Prostate Cancer. Eur Urol 2015; 68:464-470.