Enhanced specificity for CIN2+ disease detection as a reflex option

The Evolution of HPV Testing
The link between high-risk HPV (HR HPV) and the development of cervical cancer has been well established in numerous publications during the past decade. High-risk HPV clinical studies continue to provide scientific data used to generate clinical practice guidelines. Most recently, the American Society for Colposcopy and Cervical Pathology has recommended genotyping for viral strains HPV 16 and HPV 18 to categorize and stratify patients for immediate intervention.1

As a result of continued research, multiple peer-reviewed publications have linked the overexpression of HPV oncoproteins E6 and E7 to the progression of cervical disease. This overexpression plays a significant role in the growth of malignant cervical cells by shutting down tumor suppressors and proteins.2-4 The overexpression of E6 and E7 in an individual cell is the molecular engine that leads to cervical cancer. Therefore, detection may help identify infection more likely to progress to disease.4,5

mRNA HPV Biomarker and Clinical Gaps in Cervical Cancer Screening
While HR HPV DNA testing has been shown to have excellent sensitivity and negative predictive value, the specificity has been shown to be much lower than cytology, affecting positive predictive value.4,5 mRNA testing for E6/E7 offers an improvement in specificity and positive predictive value for transforming infections (CIN2+ disease).4,6

HPV E6/E7 QuantaSURE® – An mRNA-based Test
The HPV E6/E7 QuantaSURE HPV test uses flow cytometry to differentiate cell types within a sample, measure the quantity of E6/E7 mRNA per cell, and calculate the percentage of cells that are overexpressing E6/E7 mRNA. The quantification of E6 and E7 in the cells helps to triage women for disease progression, helps to identify high-grade lesions, and to identify those women at increased risk for cervical disease.4,5,6 The detection of E6/E7 is not just a sign of virus within the cell but evidence of viral activity. Data have demonstrated that E6 and E7 mRNA may help in discriminating the presence of ≥ CIN2 disease.4


Figure 1.
Progression scheme depicting the stages leading to the development of cervical cancer from HPV infection to invasive disease. A. Functional progression model. B. Morphology based description of progression; arrows, HPV oncogene expression. C. Representative p16 staining patterns associated with morphologic and functional disease stages.

HPV E6/E7 QuantaSURE®
- Correlation to disease with a PPV of 78% vs DNA testing PPV of 43% in cells for CIN2+.
- Offers clinical sensitivity that is equivalent to high-risk HPV DNA tests (>90% detection of ≥ CIN2).
- Provides an increase in specificity (clinical results in the US on 600 biopsy-confirmed samples show the clinical specificity for CIN2+ was 86% vs 16% for cytology/HPV DNA alone).
- Quantifies the number of ectocervical and endocervical cells and the presence of obscuring inflammatory cells.
- Increase in specificity for disease does not decrease sensitivity/negative predictive value (NPV).
- Specimens accepted in either ThinPrep® or SurePath® vials.

HPV E6/E7 QuantaSURE® – Utility as a Reflex Option
- ASC-US or LSIL Pap, HPV (+) reflex to HPV E6/E7 QuantaSURE.
- Pap (-), HPV (+) reflex to HPV E6/E7 QuantaSURE.
- Pap (-), HPV (+) reflex to HPV 16/18 plus HPV E6/E7 QuantaSURE.

HPV E6/E7 QuantaSURE® Test Options

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<thead>
<tr>
<th>Test No.</th>
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<tbody>
<tr>
<td>507900</td>
<td>Human Papillomavirus (HPV) E6/E7 (QuantaSURE®)</td>
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<tr>
<td>199400</td>
<td>Gynecologic Pap Test (Image-guided), Liquid-based Preparation With Reflex to Human Papillomavirus (HPV) DNA When ASC-U or LSIL and Reflex to HPV E6/E7 (QuantaSURE®)</td>
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<td>Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus, NAA With Reflex to Human Papillomavirus (HPV) DNA When ASC-U or LSIL and Reflex to HPV E6/E7 (QuantaSURE®)</td>
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<td>Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus/Trichomonas, NAA With Reflex to Human Papillomavirus (HPV) DNA When ASC-U or LSIL and Reflex to HPV E6/E7 (QuantaSURE®)</td>
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<td>199415</td>
<td>Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Human Papillomavirus (HPV) DNA With Reflex to Genotypes 16 and 18 and HPV E6/E7 (QuantaSURE®)</td>
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<td>Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Human Papillomavirus (HPV) DNA With Reflex to HPV E6/E7 (QuantaSURE®)</td>
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</tr>
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Visit the online Test Menu at www.LabCorp.com for full test information, including CPT codes and specimen collection requirements.

References
4. Coquillard G, Patterson BK. Quantification of intracellular HPV E6/E7 mRNA expression increases the specificity and positive predictive value of cervical cancer screening compared to HPV DNA. Gyn Onc. 2011;120:89-93.
10. Karakitsos P. Molecular and immunochemical biomarkers in the triage of ASCUS/LSIL and HSIL category. Presentation presented at: Eurogin International Multidisciplinary Congress; November 3-6, 2013; Florence, Italy.