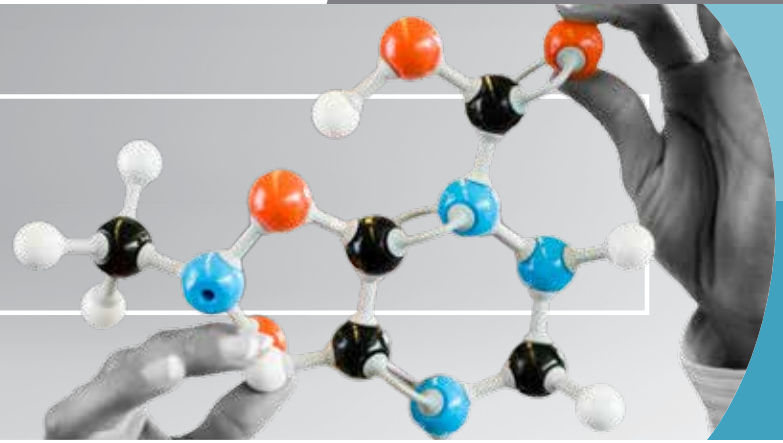


HPV E6/E7 QuantaSURE®

Helping you provide better patient care



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.^{4,5,6,7} 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 \geq CIN2 disease.⁴

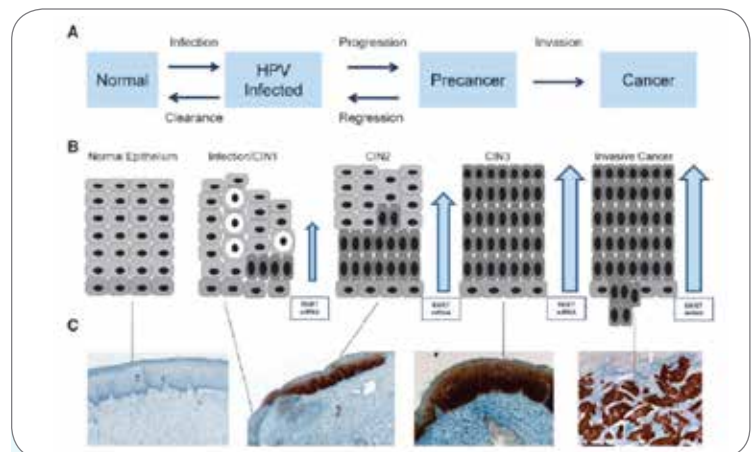


Figure 1.

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 oncoprotein expression. **C.** Representative p16 staining patterns associated with morphologic and functional disease stages.

Reprinted by permission from the American Association for Cancer Research: Cuschieri K, Wentzensen N. Human papillomavirus mRNA and p16 detection as biomarkers for the improved diagnosis of cervical neoplasia. *Cancer Epidemiol Biomarkers Prev.* 2008 Oct;17(10):2536-2545. doi: 10.1158/1055-9965.EPI-08-0306.

NO TWO PATIENTS ARE ALIKE

HPV E6/E7 QuantaSURE®

- Correlation to disease with a PPV of 78% vs DNA testing PPV of 43% in cells for CIN2+⁴
- Offers clinical sensitivity that is equivalent to high-risk HPV DNA tests (>90% detection of \geq CIN2)^{4,8}
- 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)⁹
- 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)¹⁰
- 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

Test No.	Test Name
507900	Human Papillomavirus (HPV) E6/E7 (QuantaSURE®)
199400	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®)
199405	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®)
199410	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus/ <i>Trichomonas</i> , NAA With Reflex to Human Papillomavirus (HPV) DNA When ASC-U or LSIL and Reflex to HPV E6/E7 (QuantaSURE®)
199415	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®)
199420	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus, NAA and Human Papillomavirus (HPV) DNA With Reflex to Genotypes 16 and 18 and HPV E6/E7 (QuantaSURE®)
199425	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus/ <i>Trichomonas</i> , NAA and Human Papillomavirus (HPV) DNA With Reflex to Genotypes 16 and 18 and HPV E6/E7 (QuantaSURE®)
199430	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Human Papillomavirus (HPV) DNA with Reflex to HPV E6/E7 (QuantaSURE®)
199435	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus, NAA and Human Papillomavirus (HPV) DNA With Reflex to HPV E6/E7 (QuantaSURE®)
199440	Gynecologic Pap Test (Image-guided), Liquid-based Preparation and Chlamydia/Gonococcus/ <i>Trichomonas</i> , NAA and Human Papillomavirus (HPV) DNA With Reflex to HPV E6/E7 (QuantaSURE®)

Visit the online Test Menu at www.LabCorp.com for full test information, including CPT codes and specimen collection requirements.

References

1. Massad LS, Einstein MH, Huh WK, et al. American Society for Colposcopy and Cervical Pathology. 2012 Updated Consensus Guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Journal of Lower Genital Tract Disease*. 2013;17(5):S1-S27.
2. Hausen HZ. Papillomaviruses and cancer: from basic studies to clinical application. *Nature*. 2002 May (2):342-350.
3. Cuschieri K, Wentzensen N. Human papillomavirus mRNA and p16 detection as biomarkers for the improved diagnosis of cervical neoplasia. *Cancer Epidemiol Biomarkers Prev*. 2008 October;17(10):2536-2545.
4. Coquillard G, Palao B, 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.
5. Spathis A, Kottaridi C, Chranioti A, et al. mRNA and DNA detection of human papillomavirus in women of all ages attending two colposcopy clinics. *PLOS One*. 2012 Nov;7(11):1-9.
6. Piery D et al. Intracellular human papillomavirus E6, E7 mRNA quantification predicts CIN2+ in cervical biopsies better than Papanicolaou screening for women regardless of age. *Arch Pathol Lab Med*. 2012 Aug;136:956-960.
7. Narimatsu R, Patterson BK. High-throughput cervical cancer screening using intracellular human papillomavirus E6 and E7 mRNA quantification by flow cytometry. *Am J Clin Path*. 2005;123:716-723.
8. Coquillard G, Patterson BK. High-throughput E6,E7 mRNA quantification in cervical cancer screening using flow cytometry increases specificity for CIN2+ lesions and can differentiate pre-squamous cell carcinoma from pre-adenocarcinoma. HPV Today Newsletter. 2012 September. No. 26. Available at www.hpvtoday.com.
9. Patterson BK, Chargin A, Penfold-Brown D, Shults K. From bedside to laboratory: Highly sensitive discrimination of cervical cancer markers using "The Slideless Pap" parameters and bioinformatics. Presentation presented at: Eurogin International Multidisciplinary Congress; November 3-6, 2013; Florence, Italy.
10. Karakitsos P. Molecular and immunocytochemical biomarkers in the triage of ASCUS/LSIL and HSIL category. Presentation presented at: Eurogin International Multidisciplinary Congress; November 3-6, 2013; Florence, Italy.



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