



## *A New Preventative Strategy for Cervical Cancer*

# Human Papillomavirus (HPV) Testing by Digene Hybrid Capture II Assay™

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HUMAN PAPILLOMAVIRUS (HPV) is a very common viral infection. Once thought to produce only benign warts, it is now known that over 90% of cervical cancer cases are associated with one of the Intermediate/High-Risk HPV serotypes: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68.

The incidence of HPV infection peaks a few years after the onset of sexual activity, reaching a prevalence of 60% or greater in some populations. Most of these infections are asymptomatic and regress spontaneously. However, about 5% will develop cytologic abnormalities – mostly low-grade squamous intraepithelial lesions (low-grade SIL). Of these women, about 10% will develop a *persistent* HPV infection that can progress to high-grade SIL and possibly to invasive squamous carcinoma. A few women will even progress directly to these more serious abnormalities without an intervening “low-grade” step.

The intense interest in HPV has led to the development of a sensitive and specific test for the detection of HPV DNA in infected cells, the *Digene Hybrid Capture II Assay*. The value of this test in the evaluation of women with equivocal Pap smear results was recently demonstrated in a large, carefully controlled study sponsored by the National Cancer Institute. This study (known as “ALTS” for ASCUS/Low-Grade SIL Triage Study) evaluated the usefulness of HPV testing in women whose Pap smears contained either atypical squamous cells of uncertain significance (ASCUS) or low-grade SIL.

### Highlights of ALTS

- Approximately 11% of women with an original diagnosis of ASCUS were eventually found to have high-grade SIL or worse on colposcopy. These are the patients who need to be detected and treated.
- Of the women with high-grade SIL or worse, 96% tested positive for high-risk HPV. Only 85% of these women would have been detected by repeat cytology.
- Of the women with ASCUS who were later shown *not* to have high-grade SIL or worse, 99% had a negative HPV test.
- The study concluded that HPV testing of patients with a cytological diagnosis of ASCUS is highly effective in detecting those with a significant underlying abnormality (i.e., high-grade SIL or worse).
- Of women with an original cytological diagnosis of low-grade SIL, over 80% had a positive HPV test. Thus, the molecular assay had little effect on clinical decision making for this group. The study concluded that patients with a cytological diagnosis of low-grade SIL do *not* benefit from HPV triage testing, and are best managed by immediate colposcopy/biopsy.

### QUICK FACTS

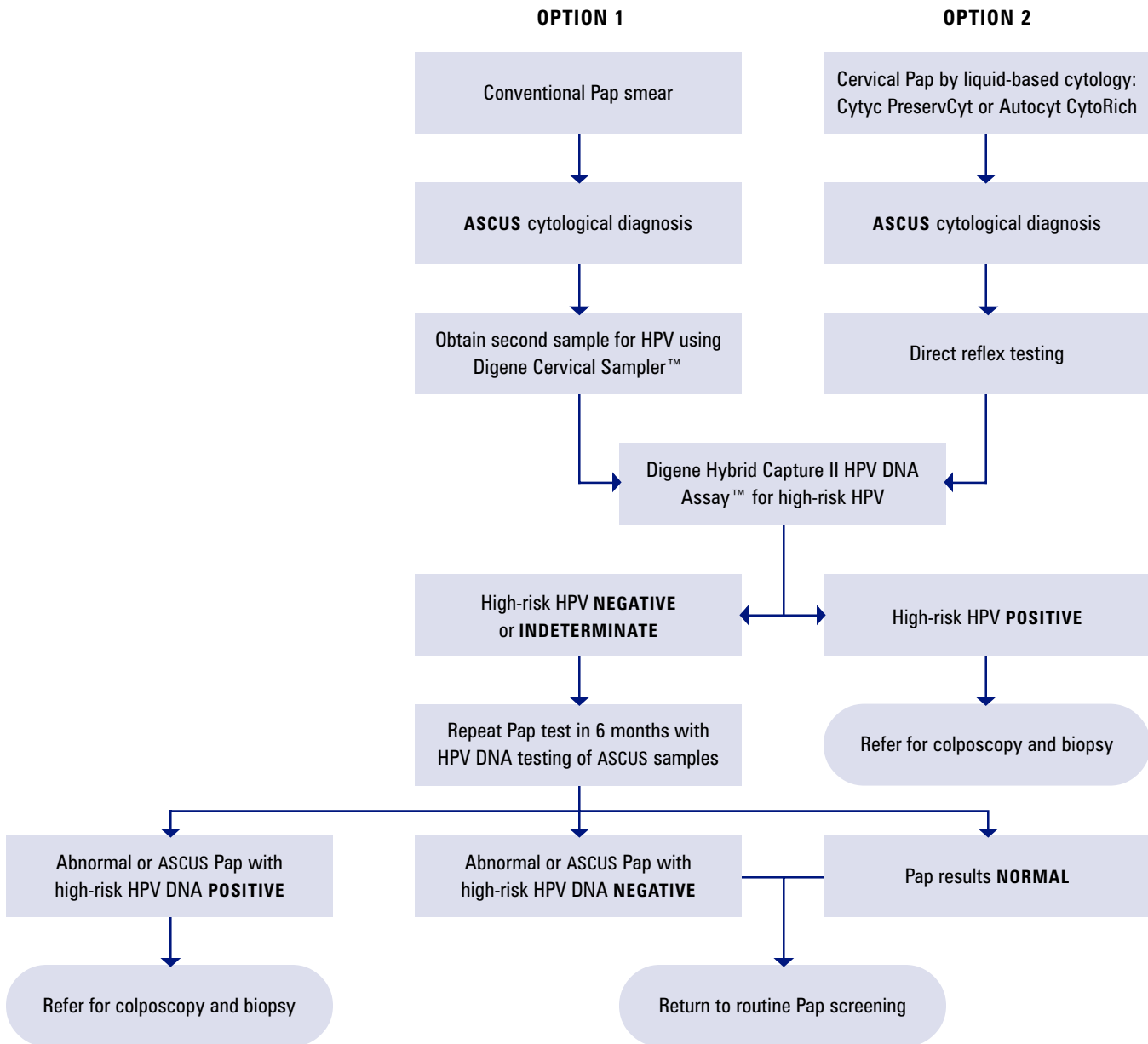
#### Digene HPV DNA by Hybrid Capture

- ▶ **Highly effective in women with ASCUS Pap smear results to assess the need for colposcopy**
- ▶ **Can be preformed as a reflexive test on ASCUS Pap smears collected in Cytoc PreservCyt® or Autocyte liquid-based cytology media**
- ▶ **Negative predictive value >99%**
- ▶ **Sensitivity >95%**
- ▶ **Order Intermediate/High-Risk probe only (Types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) or Intermediate/High-Risk and Low-Risk (Types: 6, 11, 42, 43, and 44) probes**
- ▶ **Test differentiates between Intermediate/High-Risk and Low-Risk HPV but cannot determine specific HPV serotypes.**

**For more information, please contact Client Services.**

**Cervical cells for HPV DNA testing may be sent in one of two ways**

- **Option 1:** Digene Cervical Sampler™ following an ASCUS diagnosis on a routine Pap smear. (Requires a second patient visit.)
- **Option 2:** Cytoc PreservCyt® or Autocyte CytoRich® for liquid-based cytological examination with reflex HPV testing if indicated. (Only one collection is needed, and it assures that testing is done only on samples known to contain atypical cells.)



**Selected References**

1. Cox, JT, et al. Human papillomavirus testing by hybrid capture appears to be useful in triaging women with cytologic diagnosis of atypical squamous cells of undetermined significance. *Am J Obstet Gynecol* 1995;172:946-954
2. Manos, MM, et al. Identifying women with cervical neoplasia using Human papillomavirus DNA testing for equivocal Papanicolaou results. *JAMA* 1999;281:1605-1610.
3. Human papillomavirus testing for triage of women with cytologic evidence of low-grade squamous intraepithelial lesions: baseline data from randomized trial. The Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesions Triage Study (ALTS) Group. *J Natl Cancer Inst* 2000;92(5):397-402.
4. Solomon, D, et al. Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: Baseline results from a randomized trial. *J Natl Cancer Inst* 2001;93(4):293-299.

## Test Information

DESCRIPTION	<b>HPV DNA PROBE HIGH &amp; LOW RISK</b>
METHOD	Nucleic Acid Probe
ORDER CODE	HPVHC
CPT CODE	87621 × 2
SPECIMEN	Cervical specimens collected and transported using Digene Cervical Sampler (brush) and specimen transport medium, or cervical and endocervical sample collected using the ThinPrep Pap Test® or Autocyte CytoRich® specimen transport medium. Specimens must be transported in the proper transport medium. Store and transport refrigerated. Indicate specimen source.
COMMENTS	<p><i>Minimum amount:</i> 4 mL of ThinPrep Pap Test solution remaining after the Pap test has been prepared.</p> <p><i>Unacceptable conditions:</i> Samples in EIA transport media, wooden swabs, and male samples.</p> <p><i>Stability:</i> Digene: 2 weeks at room temperature, 3 weeks refrigerated, 3 months frozen. ThinPrep and Autocyte: 3 weeks at room temperature, 3 weeks refrigerated, <b>DO NOT FREEZE</b>.</p>
SCHEDULE	Monday and Thursday evenings
TURNAROUND	3-5 days
RANGES	<b>Source</b> <b>High-Risk HPV</b> Negative <b>Low-Risk HPV</b> Negative Studies have shown an association between certain HPV genotypes and some anogenital diseases. HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 comprise the “high-risk” group and are associated with cervical carcinoma and its characteristic lesions; cervical atypia, severe dysplasia, cervical intraepithelial neoplasia (CIN), and carcinoma in situ. The HPV test should be used only to augment existing methods for the detection of cervical disease. Its results should be interpreted in conjunction with relevant clinical information from other diagnostic and screening tests, physical examinations, and full medical history. HPV types 6, 11, 42, 43, and 44 are considered the “low-risk” group and are associated with benign condylomas (warts). Results are reported by group only. The Digene Hybrid Capture HPV Assay cannot determine specific HPV genotypes.

DESCRIPTION	<b>HPV DNA PROBE HIGH RISK</b>
METHOD	Nucleic Acid Probe
ORDER CODE	HPVHR
CPT CODE	87621
SPECIMEN	Cervical specimens collected and transported using Digene Cervical Sampler (brush) and specimen transport medium, or cervical and endocervical sample collected using the ThinPrep Pap Test or Autocyte CytoRich specimen transport medium. Specimens must be transported in the proper transport medium. Store and transport refrigerated. Indicate specimen source.
COMMENTS	<p><i>Minimum amount:</i> 4 mL of ThinPrep Pap Test solution remaining after the Pap test has been prepared.</p> <p><i>Unacceptable conditions:</i> Samples in EIA transport media, wooden swabs, and male samples.</p> <p><i>Stability:</i> Digene: 2 weeks at room temperature, 3 weeks refrigerated, 3 months frozen. ThinPrep and Autocyte: 3 weeks at room temperature, 3 weeks refrigerated, <b>DO NOT FREEZE</b>.</p>
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