Human Papillomavirus (HPV) DNA Detection with Genotyping, High Risk Types by PCR, ThinPrep

Useful For
- Detection of high risk (HR) genotypes associated with the development of cervical cancer
- An aid in triaging women with abnormal Pap smear results
- Individual genotyping of human papillomavirus (HPV)-16 and/or HPV-18, if present
- Results of HPV-16 and HPV-18 genotyping can be used as an aid in triaging women with positive HR-HPV but negative Pap smear results.

Clinical Information
Persistent infection with human papillomavirus (HPV) is the principal cause of cervical cancer and its precursor cervical intraepithelial neoplasia (CIN). (1-3) The presence of HPV has been implicated in >99% of cervical cancers worldwide. HPV is a small, non-enveloped, double-stranded DNA virus, with a genome of approximately 8,000 nucleotides. There are more than 118 different types of HPV and approximately 40 different HPVs that can infect the human anogenital mucosa. However, data suggest that 14 of these types (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are considered high risk (HR) for the development of cervical cancer and its precursor lesions. Furthermore, HPV types 16 and 18 have been regarded as the genotypes most closely associated with progression to cervical cancer. HPV-16 is the most carcinogenic, and is associated with approximately 60% of all cervical cancers, while HPV-18 accounts for approximately 10% to 15% of cervical cancers. (1-3)

Although persistent infection with HR HPV is necessary for the development of cervical cancer and its precursor lesions, only a very small percentage of infections progress to these disease states. Sexually transmitted infection with HPV is extremely common, with estimates of up to 75% of all women being exposed to HPV at some point. However, almost all infected women will mount an effective immune response and clear the infection within 2 years without any long term health consequences. An infection with any HPV type can produce CIN although this also usually resolves once the HPV infection has been cleared.

In developed countries with cervical cancer screening programs, the Pap smear has been used since the mid-1950s as the primary tool to detect early precursors to cervical cancer. Although it has decreased the death rates due to cervical cancer dramatically in those countries, the Pap smear and subsequent liquid based cytology methods require subjective interpretation by highly trained cytopathologists and misinterpretation can occur. Cytological abnormalities are primarily due to infection with HPV; however, various inflammatory conditions or sampling variations can result in false positive cytology results. Triage of an abnormal cytology result may involve

Reference Values
Negative for HPV genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68

Analytic Time
3 day
repeat testing, colposcopy and/or biopsy. A histologically confirmed high-grade lesion must be surgically removed or ablated in order to prevent the development of invasive cervical cancer.

Nucleic acid (DNA) testing by PCR has become a standard, noninvasive method for determining the presence of a cervical HPV infection. Proper implementation of nucleic acid testing for HPV may 1) increase the sensitivity of cervical cancer screening programs by detecting high-risk lesions earlier in women 30 years and older with normal cytology and 2) reduce the need for unnecessary colposcopy and treatment in patients 21 and older with cytology results showing atypical squamous cells of undetermined significance (ASC-US).

Recently, data suggest that individual genotyping for HPV types 16 and 18 can assist in determining appropriate follow-up testing and triaging women at risk for progression to cervical cancer. Studies have shown that the absolute risk of CIN-2 or worse in HPV-16 and/or HPV-18 positive women is 11.4% (95% confidence interval [CI] 8.4%-14.8%) compared with 6.1% (95% CI, 4.9%-7.2%) of women positive for 'other' HR-HPV genotypes and 0.8% (95% CI, 0.3%-1.5%) in HR-HPV negative women.(4) Based in part on these data, the American Society for Colposcopy and Cervical Pathology (ASCCP) now recommends that HPV 16/18 genotyping be performed on women that are positive for HR-HPV but negative by routine cytology. Women that are found to be positive for HPV-16 and/or -18 may be referred to colposcopy, while women that are negative for genotypes 16 and/or 18 may have repeat cytology and HR HPV testing in 12 months.(1)

**Interpretation**

A positive result indicates the presence of human papillomavirus (HPV) DNA due to 1 or more of the following genotypes: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.

A negative result indicates the absence of HPV DNA of the targeted genotypes.

For patients with atypical squamous cells of undetermined significance (ASC-US) Pap smear result and who are positive for high-risk (HR) HPV, consider referral for colposcopy, if clinically indicated.

For women aged 30 years and older with a negative Pap smear result but who are positive for HPV-16 and/or HPV-18, consider referral for colposcopy, if clinically indicated.

For women aged 30 years and older with a negative Pap smear, positive HR HPV test result, but who are negative for HPV-16 and HPV-18, consider repeat testing by both cytology and a HR HPV test in 12 months.

**Cautions**

The cobas human papillomavirus (HPV) test is FDA-approved for cervical/endocervical samples collected in PreservCyt (ThinPrep) media. Other sample types (eg, vaginal) are not considered FDA-approved sources; however, verification studies have been completed in compliance with CLIA-regulations by Mayo Medical Laboratories.

The cobas HPV test detects DNA of the high-risk types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. This test does not detect DNA of HPV low-risk types (eg, 6, 11, 42, 43, 44) since these are not associated with cervical cancer and its precursor lesions.

The cobas HPV test is not recommended for evaluation of suspected sexual abuse.

Prevalence of HPV infection in a population may affect performance. Positive predictive values decrease when testing populations with low prevalence or individuals with no risk of infection.

Infection with HPV is not an indicator of cytologic high grade intraepithelial lesion (HSIL) or underlying high-grade cervical intraepithelial neoplasia (CIN), nor does it imply that CIN2-3 or cancer will develop. Most women infected with 1 or more high-risk (HR) HPV types do not develop CIN2-3 or cancer.

A negative HR HPV result does not exclude the possibility of future cytologic HSIL or underlying CIN2-3 or cancer.

**Clinical References**


5. Procedure manual and package insert: cobas HPV test. Roche Diagnostics. Indianapolis, IN, version 05641268001-01EN