New FDA-Approved HPV Test Improves Detection of High Risk Genotypes

**BENEFITS**

- The only clinically validated, FDA-approved assay that simultaneously provides individual results on the highest-risk genotypes – HPV16 and HPV18 – and a pooled result on the 12 other high-risk HPV genotypes
- No extra cost for HPV 16/18 genotyping with positive HPV
- Detects HPV DNA
- Small sample size (1 mL) helps eliminate patient call backs due to Quantity-Not-Sufficient results
- Ancillary tests are available from the same vial: *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis*

**LIMITATIONS**

- FDA-approved for ThinPrep collection method only. There is no FDA-approved HPV test from the SurePath vial

**SUMMARY**

PeaceHealth Laboratories introduces new U.S. Food and Drug Administration-approved testing for high-risk Human Papillomavirus testing and HPV 16/18 genotyping using the Roche cobas® HPV assay and instrumentation.

In addition to HPV DNA and genotyping, testing for *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis* are available from the same vial.

**NATIONAL GUIDELINES RECOMMEND CO-TESTING PAP AND HPV**

HPV is a species of virus made up of over 100 subtypes, some of which cause genital warts and some of which are linked to cervical changes and cancer of the cervix, vulva, vagina, penis, anus and throat. HPV is the most common sexually transmitted infection and is the cause of almost all cervical cancers, which are the second most common cancer among women (see Figure 1, page 2).

To help prevent the onset of disease, nationally-recognized health governing bodies (see Figure 4, page 4) recommend routine Pap and HPV co-testing for women ≥ age 30 to identify those most likely to develop cervical cancer.

These guidelines were updated in 2012 and are consistent across the following: American Congress of Obstetricians and Gynecologists (ACOG), American Society for Clinical Pathology (ASCP), American Cancer Society (ACS), American Society for Colposcopy and Cervical Pathology (ASCCP) and United States Preventive Services Task Force (USPSTF).

**DETECTS HIGH-RISK GENOTYPES**

The Roche cobas® HPV test detects 14 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) that cause more than 95% of cervical squamous cell carcinoma and its precursors, and in excess of 90% of true cervical adenocarcinoma and its precursor, adenocarcinoma in situ.
New FDA-Approved HPV Test Improves Detection of High Risk Genotypes (continued)

**Figure 1: Estimated Number of New/Existing (Total) Sexually Transmitted Infections (United States, 2008)**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>117,000</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>270,000</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>422,000</td>
</tr>
<tr>
<td>HIV</td>
<td>908,000</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>1,570,000</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>3,710,000</td>
</tr>
<tr>
<td>HSV-2</td>
<td>24,100,000</td>
</tr>
<tr>
<td>HPV</td>
<td>79,100,000</td>
</tr>
</tbody>
</table>

**Total: 110,197,000**

*Gender totals do not equal overall total, due to rounding. Bars are for illustration only; not to scale, due to wide range in numbers of infections.*

**HPV 16 AND 18 GENOTYPING ADDS SPECIFICITY AND FURTHER DEFINES RISK**

Approximately 70% of cervical cancers worldwide are due to types 16 and 18.\(^2\) The risk of developing cervical cancer or precancer (grade 3 cervical intraepithelial neoplasia [CIN3]) is increased with the HPV genotypes 16 and 18 (see Figure 2).

The American Society for Colposcopy and Cervical Pathology 2012 Consensus Guidelines recommend molecular genotyping assays to be clinically useful for cytology-negative women > age 30 years who are HPV DNA positive to determine which women:

- should be referred for immediate colposcopy
- could be followed-up with repeat cytology and high-risk HPV testing in 12 months

**Figure 2: HPV 16/18 Genotyping ATHENA Trial Results**

<table>
<thead>
<tr>
<th>HPV Status</th>
<th>Cumulative Incidence Rate, % (Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 16+</td>
<td>25.2% (21.7, 28.7)</td>
</tr>
<tr>
<td>HPV 18+</td>
<td>11.0% (7.1, 15.4)</td>
</tr>
<tr>
<td>12 Other HR+</td>
<td>5.4% (4.5, 6.4)</td>
</tr>
<tr>
<td>HPV-</td>
<td>0.3% (0.1, 0.7)</td>
</tr>
</tbody>
</table>

Women who were HPV 16 or 18 positive at baseline were at the highest risk of developing high-grade cervical disease over a three-year period (ATHENA primary screening population ≥ 25 years).
The ASCCP released an updated management algorithm in 2012 to manage HPV high-risk positive/cytology-normal women ≥ age 30 years (see Figure 3). The ASCCP determined that HPV 16 and 18 genotype testing would be clinically useful for women ≥ age 30 years with normal cytology that test positive for high-risk HPV.

**WHY ROCHE COBAS?**

**Improved HPV Specificity**

Improved specificity translates into fewer false positive screening results, saving patients undue anxiety and unnecessary follow-up diagnostic procedures.

**Reduced Quantity-Not-Sufficient Results**

The new instrument uses a very small amount of specimen to perform many tests, greatly reducing the incidence of quantity not sufficient results.

**Rapid Turnaround Time**

HPV 16/18 genotyping takes place during co-testing and is resulted at no additional cost when there is a positive HPV result.

**FDA Approved**

Nationally-recognized guidelines specify that HPV testing should be FDA-approved. The FDA has approved the Roche cobas® high risk HPV DNA test to:

1. Triage women with atypical cells of undetermined significance (ASC-US) Pap test results.
2. Use as an adjunct to the Pap test to screen for cervical cancer in women ≥ age 30.
3. Use as a first-line primary screening test for cervical cancer in women ≥ age 25.

The Roche cobas® HPV Test was clinically validated in the ATHENA trial, the largest U.S.-based study for cervical cancer screening. It is the only FDA-approved test for use as a first-line primary screening test for cervical cancer in women ≥ age 25, though current guidelines do not recommend HPV testing alone as a first-line primary screening tool.

**QUESTIONS?**

Mark Endicott, MS, CT(ASCP)
Manager, Anatomic Pathology for Oregon and Vancouver, Washington
☎ 800-826-3616 ext. 1569
☎ 541-556-9128
mendicott@peacehealthlabs.org

Mohiedean Ghofrani, MD, MBA
Director, Cytopathology and Women’s Health, Vancouver
☎ 360-514-2708
mghofrani@peacehealthlabs.org

Robert Liao, PhD, D(ABMM)
Director, Microbiology, Serology and Molecular Diagnostics
☎ 541-687-2134 ext. 4798
☎ 800-826-3616 ext. 4798
rliao@peacehealthlabs.org

John DiTomasso, MD
Medical Director, Cytopathology Northwest Pathology Services Pathology Consultants
☎ 541-984-8284
jditomasso@pathconsultants.com

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Figure 4: Summary of 2012 ACOG, ASCP, ACS, and ASCCP Nationally Recognized Cervical Cancer Screening Guidelines for Women of Average Risk

<table>
<thead>
<tr>
<th>Age</th>
<th>Screening Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 21 years</td>
<td>No cervical cancer screening of any kind</td>
<td>HPV testing should not be used for screening or ASC-US reflex in this age group. Recommended screening practices should not change on the basis of HPV vaccination status.</td>
</tr>
<tr>
<td>21 - 29 years</td>
<td>Cytology alone primary screening every three years (acceptable) HPV testing with cytology ASC-US findings (preferred)</td>
<td>Routine HPV cotesting is not recommended in this age group. HPV testing is recommended in cases of ASC-US cytology.</td>
</tr>
<tr>
<td>30 - 65 years</td>
<td>HPV and cytology cotesting every five years (preferred)</td>
<td>Screening by HPV testing alone is not recommended for most clinical settings.</td>
</tr>
<tr>
<td>Over 65 years</td>
<td>No screening following adequate history of negative prior screening</td>
<td>Women with history of &gt;CIN 2 should continue screening for at least 20 years.</td>
</tr>
<tr>
<td>After hysterectomy</td>
<td>No screening if no previous history of &gt;CIN 2</td>
<td>Continue screening (cytology) if there is history of &gt;CIN 2 in the past 20 years or cervical cancer ever.</td>
</tr>
</tbody>
</table>

NOTE: A more complete summary of these recommendations is available at http://www.cdc.gov/cancer/cervical/pdf/guidelines.pdf

ORDERING INFORMATION

Oregon
68338  HPV HR & 16/18 Genotype (ThinPrep)
70073  Cytopathology, ThinPrep PAP with HPV High Risk, if ASCUS
70074  Cytopathology, ThinPrep Pap with HPV, High Risk, if Abnormal
70066  Cytopathology, ThinPrep Pap with HPV (30 Years and Older)

Vancouver, Washington
68338  HPV HR & 16/18 Genotype (ThinPrep)

SPECIMEN REQUIREMENTS

Handling: Label ThinPrep vial with patient name (first and last), physician name
Stability: Specimen in ThinPrep preservative fluid stable 30 days ambient
CPT Code: 87621 x 1

REFERENCES